

## Supplementary Online Content

Uldrick TS, Gonçalves PH, Abdul-Hay M, et al. Assessment of the safety of pembrolizumab in patients with HIV and advanced cancer: a phase 1 study. Published online June 2, 2019. *JAMA Oncol*. doi:10.1001/jamaoncol.2019.2244

**eTable 1.** Demographics and Baseline Characteristics

**eTable 2.** Treatment Emergent Adverse Events at Least Possibly Related to Pembrolizumab, Worst per Patient

**eTable 3.** All Treatment Emergent Serious Adverse Events by Study Cohort

**eTable 4.** All Treatment Emergent Adverse Events by Cohort

**eFigure 1.** Liver biopsy in participant with sarcomatoid lung cancer with large metastases to liver who developed immune related AST/ALT after administration of pembrolizumab

**eFigure 2.** Autopsy findings in participant who died of Kaposi sarcoma herpesvirus associated polyclonal B-cell lymphoproliferation

**eFigure 3.** 18-fluorodeoxyglucose positron emission tomography in participant with chemotherapy-refractory primary effusion lymphoma demonstrating improvement after pembrolizumab

This supplementary material has been provided by the authors to give readers additional information about their work.

**eTable 1. Demographics and Baseline Characteristics**

		<b>Cohort 1 CD4 100-199 cells/μL</b>	<b>Cohort 2 CD4 200 -350 cells/μL</b>	<b>Cohort 3 CD4 &gt;350 cells/μL</b>	<b>Total</b>
<b>Overall</b>	Number	6	12	12	30
<b>Age (years)</b>	Median	53	54	58	57
	Min, Max	39, 68	43, 77	42, 71	39, 77
<b>Sex</b>	Female	0	1 ( 8%)	1 ( 8%)	2 ( 7%)
	Male	6 ( 100%)	11 ( 92%)	11 ( 92%)	28 ( 93%)
<b>Race</b> <sup>1</sup>	White	4 ( 67%)	9 ( 75%)	5 ( 42%)	18 ( 60%)
	Black or African American	1 ( 17%)	3 ( 25%)	5 ( 42%)	9 ( 30%)
	Native Hawaiian or other Pacific Islander	1 ( 17%)	0	0	1 ( 3%)
	American Indian or Alaska Native	0	1 ( 8.3%)	0 ( 0.0%)	1 ( 3%)
	Unknown	0	0	2 ( 17%)	2 ( 7%)
<b>Ethnicity</b>	Hispanic or Latino	0	1 ( 8%)	2 ( 17%)	3 ( 10%)
	Not Hispanic or Latino	6 ( 100%)	11 ( 92%)	9 ( 75%)	26 ( 87%)
	Not Reported	0	0	1 ( 8%)	1 ( 3%)
<b>CD4+ T-cells/μL</b>	Median	153	227	516	285
	Min, Max	132, 184	204, 343	351, 966	132, 966
<b>HIV Viral Load</b> <sup>2</sup>	Detected	0	2 ( 17%)	2 ( 17%)	4 ( 13%)
	Not Detected	6 ( 100%)	10 ( 83%)	10 ( 83%)	26 ( 87%)
<b>ECOG Performance Status</b>	0	2 ( 33%)	6 ( 50%)	8 ( 67%)	16 ( 53%)
	1	4 ( 67%)	6 ( 50%)	4 ( 33%)	14 ( 47%)
<b>Cancers</b>		6 ( 100%)	12 ( 100%)	12 ( 100%)	30 ( 100%)
<b>AIDS Defining</b>		1 ( 17%)	4 ( 33%)	6 ( 50%)	11 ( 37%)

	Kaposi Sarcoma	0	2 ( 17%)	4 ( 33%)	6 ( 20%)
	Diffuse Large B-Cell Lymphoma	0	1 ( 8%)	2 ( 17%)	3 ( 10%)
	Primary Effusion Lymphoma	1 ( 17%)	1 ( 8%)	0	2 ( 7%)
<b>Non-AIDS Defining</b>		5 ( 83%)	8 ( 67%)	6 ( 50%)	19 ( 63%)
	Anal	4 ( 67%)	2 ( 17%)	0	6 ( 20%)
	Skin, Squamous Cell	1 ( 17%)	1 ( 8%)	1 ( 8%)	3 ( 10%)
	Adenoid cystic Carcinoma	0	0	1 ( 8%)	1 ( 3%)
	Bladder	0	0	1 ( 8%)	1 ( 3%)
	Cholangiocarcinoma	0	1 ( 8%)	0	1 ( 3%)
	Hepatocellular	0	1 ( 8%)	0	1 ( 3%)
	Non-Small Cell Lung	0	1 ( 8%)	0	1 ( 3%)
	Pancreatic	0	0	1 ( 8%)	1 ( 3%)
	Papillary Urothelial Carcinoma	0	0	1 ( 8%)	1 ( 3%)
	Prostate	0	1 ( 8%)	0	1 ( 3%)
	Sarcomatoid Lung	0	0	1 ( 8%)	1 ( 3%)
	Tonsillar	0	1 ( 8%)	0	1 ( 3%)
<b>Prior Systemic Therapy</b>	Median	3	3	2	2
	Min, Max	1, 4	1, 8	0, 5	0, 8
<b>Prior radiation</b>		5 ( 83%)	11 ( 92%)	3 ( 25%)	19 ( 63%)
<p>ECOG, Eastern Cooperative Oncology Group; 0, Asymptomatic and fully active; 1, Symptomatic; fully ambulatory; restricted in physically strenuous activity</p> <p>1. One participant selected more than one race</p> <p>2. Detectable defined as HIV viral load &lt; 20 copies/mL</p>					

**eTable 2. Treatment Emergent Adverse Events at Least Possibly Related to Pembrolizumab, Worst per Patient**

<b>Event</b>	<b>Grade 1</b>	<b>Grade 2</b>	<b>Grade 3</b>	<b>Total</b>
Any	6 (20%)	16 (53%)	6 (20%)	29 (97%)
<b>Blood and lymphatic system disorders</b>				
Anemia	4 (13%)	5 (17%)	4 (13%)	13 (43%)
<b>Endocrine disorders</b>				
Hypothyroidism	2 (7%)	6 (20%)	0	8 (27%)
<b>Eye disorders</b>				
Blurred vision	1 (3%)	0	0	1 (3%)
Dry eye	1 (3%)	0	0	1 (3%)
<b>Gastrointestinal disorders</b>				
Abdominal pain	4 (13%)	0	0	4 (13%)
Bloating	1 (3%)	0	0	1 (3%)
Constipation	1 (3%)	0	0	1 (3%)
Diarrhea	1 (3%)	0	0	1 (3%)
Flatulence	1 (3%)	0	0	1 (3%)
Gastroesophageal reflux disease	1 (3%)	0	0	1 (3%)
Nausea	6 (20%)	1 (3%)	0	7 (23%)
Vomiting	3 (10%)	0	0	3 (10%)
<b>General disorders and administration site conditions</b>				
Edema limbs	0	0	1 (3%)	1 (3%)
Edema trunk	0	1 (3%)	0	1 (3%)
Fatigue	7 (23%)	3 (10%)	0	10 (33%)
Fever	1 (3%)	2 (7%)	0	3 (10%)
Localized edema	0	2 (7%)	0	2 (7%)
Metallic taste in mouth	1 (3%)	0	0	1 (3%)
Pain	1 (3%)	1 (3%)	0	2 (7%)
<b>Infections and infestations</b>				
Soft tissue infection	0	1 (3%)	1 (3%)	2 (7%)
<b>Investigations</b>				
Alanine aminotransferase increased	2 (7%)	0	1 (3%)	3 (10%)

<b>Event</b>	<b>Grade 1</b>	<b>Grade 2</b>	<b>Grade 3</b>	<b>Total</b>
Alkaline phosphatase increased	4 (13%)	2 (7%)	0	6 (20%)
Aspartate aminotransferase increased	3 (10%)	0	1 (3%)	4 (13%)
Blood bilirubin increased	0	1 (3%)	0	2 (7%)
CD4 lymphocytes decreased	0	1 (3%)	1 (3%)	2 (7%)
Creatine phosphokinase increased	1 (3%)	1 (3%)	0	2 (7%)
Lymphocyte count decreased	3 (10%)	2 (7%)	1 (3%)	6 (20%)
Neutrophil count decreased	0	2 (7%)	1 (3%)	3 (10%)
Platelet count decreased	1 (3%)	1 (3%)	0	3 (10%)
Weight loss	1 (3%)	0	0	1 (3%)
White blood cell decreased	0	1 (3%)	0	1 (3%)
<b>Metabolism and nutrition disorders</b>				
Anorexia	2 (7%)	0	0	2 (7%)
Hypoalbuminemia	0	1 (3%)	0	1 (3%)
Hypocalcemia	1 (3%)	0	0	1 (3%)
Hypokalemia	1 (3%)	0	0	1 (3%)
Hyponatremia	2 (7%)	0	0	2 (7%)
<b>Musculoskeletal and connective tissue disorders</b>				
Joint stiffness	1 (3%)	0	0	1 (3%)
Pain in extremity	0	3 (10%)	0	3 (10%)
<b>Nervous system disorders</b>				
Dizziness	1 (3%)	0	0	1 (3%)
Headache	2 (7%)	0	0	2 (7%)
Tremor	0	1 (3%)	0	1 (3%)
<b>Psychiatric disorders</b>				
Insomnia	1 (3%)	0	0	1 (3%)
<b>Renal and urinary disorders</b>				
Acute kidney injury	1 (3%)	0	0	1 (3%)
GFR Decreased	0	1 (3%)	0	1 (3%)
<b>Reproductive system and breast disorders</b>				
Genital edema	0	1 (3%)	0	1 (3%)
<b>Respiratory, thoracic and mediastinal disorders</b>				
Allergic rhinitis	1 (3%)	0	0	1 (3%)
Cough	3 (10%)	0	0	3 (10%)
Dyspnea	0	1 (3%)	0	2 (7%)

<b>Event</b>	<b>Grade 1</b>	<b>Grade 2</b>	<b>Grade 3</b>	<b>Total</b>
Nasal congestion	1 (3%)	0	0	1 (3%)
Pleural effusion	0	1 (3%)	0	1 (3%)
Pneumonitis	1 (3%)	3 (10%)	0	4 (13%)
Runny nose	1 (3%)	0	0	1 (3%)
<b>Skin and subcutaneous tissue disorders</b>				
Alopecia	1 (3%)	0	0	1 (3%)
Dry skin	3 (10%)	1 (3%)	0	4 (13%)
Pruritus	5 (17%)	0	0	5 (17%)
Rash maculo-papular	3 (10%)	1 (3%)	0	4 (13%)
Skin hypopigmentation	1 (3%)	0	0	1 (3%)
Xeroderma	1 (3%)	0	0	1 (3%)
Blister mouth	1 (3%)	0	0	1 (3%)
Night sweats	1 (3%)	0	0	1 (3%)

**eTable 3. All Treatment Emergent Serious Adverse Events by Study Cohort**

<b>MedDRA System Organ Class / Preferred Term</b>	<b>Cohort 1 (N=6)</b>	<b>Cohort 2 (N=12)</b>	<b>Cohort 3 (N=12)</b>	<b>Total (N=30)</b>
<b>Number (%) of Subjects with at least one Treatment Emergent Serious Adverse Event</b>	5 ( 83.3%)	8 ( 66.7%)	6 ( 50.0%)	19 ( 63.3%)
<b>Blood and lymphatic system disorders</b>	1 ( 16.7%)	0 ( 0%)	0 ( 0%)	1 ( 3.3%)
Febrile neutropenia	1 ( 16.7%)	0 ( 0%)	0 ( 0%)	1 ( 3.3%)
<b>Eye disorders</b>	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Retinal detachment	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
<b>Gastrointestinal disorders</b>	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Abdominal pain	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
<b>General disorders and administration site conditions</b>	1 ( 16.7%)	2 ( 16.7%)	2 ( 16.7%)	5 ( 16.7%)
Death NOS	0 ( 0%)	2 ( 16.7%)	0 ( 0%)	2 ( 6.7%)
Fever	1 ( 16.7%)	0 ( 0%)	1 ( 8.3%)	2 ( 6.7%)
Edema limbs	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Edema trunk	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Failure to Thrive	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Localized edema	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Pain	0 ( 0%)	0 ( 0%)	1 ( 8.3%)	1 ( 3.3%)
<b>Infections and infestations</b>	2 ( 33.3%)	0 ( 0%)	3 ( 25%)	5 ( 16.7%)
Soft tissue infection	0 ( 0. %)	0 ( 0%)	2 ( 16.7%)	2 ( 6.7%)
Lung infection	1 ( 16.7%)	0 ( 0%)	0 ( 0%)	1 ( 3.3%)
Skin infection	1 ( 16.7%)	0 ( 0%)	0 ( 0%)	1 ( 3.3%)
Urinary tract infection	0 ( 0%)	0 ( 0%)	1 ( 8.3%)	1 ( 3.3%)
<b>Investigations</b>	1 ( 16.7%)	2 ( 16.7%)	1 ( 8.3%)	4 ( 13.3%)
Creatinine increased	1 ( 16.7%)	1 ( 8.3%)	0 ( 0%)	2 ( 6.7%)

Alanine aminotransferase increased	0 ( 0%)	0 ( 0%)	1 ( 8.3%)	1 ( 3.3%)
Aspartate aminotransferase increased	0 ( 0%)	0 ( 0%)	1 ( 8.3%)	1 ( 3.3%)
Platelet count decreased	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
<b>Metabolism and nutrition disorders</b>	0 ( 0%)	4 ( 33.3%)	0 ( 0%)	4 ( 13.3%)
Hypercalcemia	0 ( 0%)	4 ( 33.3%)	0 ( 0%)	4 ( 13.3%)
<b>Neoplasms benign, malignant and unspecified (incl cysts and polyps)</b>	2 ( 33.3%)	3 ( 25%)	1 ( 8.3%)	6 ( 20%)
Tumor pain	1 ( 16.7%)	0 ( 0%)	1 ( 8.3%)	2 ( 6.7%)
Prostate Cancer Progressive Disease	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Death due to progressive disease	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Disease progression	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Metastatic anal carcinoma	1 ( 16.7%)	0 ( 0%)	0 ( 0%)	1 ( 3.3%)
<b>Renal and urinary disorders</b>	0 ( 0%)	1 ( 8.3%)	1 ( 8.3%)	2 ( 6.7%)
Urinary retention	0 ( 0%)	1 ( 8.3%)	1 ( 8.3%)	2 ( 6.7%)
Acute kidney injury	0 ( 0%)	0 ( 0%)	1 ( 8.3%)	1 ( 3.3%)
<b>Respiratory, thoracic and mediastinal disorders</b>	0 ( 0%)	2 ( 16.7%)	0 ( 0%)	2 ( 6.7%)
Dyspnea	0 ( 0%)	2 ( 16.7%)	0 ( 0%)	2 ( 6.7%)
Pleural effusion	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
<b>Vascular disorders</b>	0 ( 0%)	1 ( 8.3%)	1 ( 8.3%)	2 ( 6.7%)
Hypotension	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Thromboembolic event	0 ( 0%)	0 ( 0%)	1 ( 8.3%)	1 ( 3.3%)



**eTable 4. All Treatment Emergent Adverse Events by Cohort**

<b>MedDRA System Organ Class / Preferred Term</b>	<b>Cohort 1 (N=6)</b>	<b>Cohort 2 (N=12)</b>	<b>Cohort 3 (N=12)</b>	<b>Total (N=30)</b>
<b>Number (%) of Subjects with at least one Treatment Emergent Adverse Event</b>	6 ( 100%)	12 ( 100%)	12 ( 100%)	30 ( 100%)
<b>Blood and lymphatic system disorders</b>	5 ( 83.3%)	11 ( 91.7%)	7 ( 58.3%)	23 ( 76.7%)
Anemia	5 ( 83.3%)	10 ( 83.3%)	7 ( 58.3%)	22 ( 73.3%)
Febrile neutropenia	1 ( 16.7%)	0 ( 0%)	0 ( 0%)	1 ( 3.3%)
Decreased Vitamin D	0 ( 0%)	2 ( 16.7%)	0 ( 0%)	2 ( 6.7%)
Increased urea nitrogen	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Thrombocytosis	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
<b>Cardiac disorders</b>	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Sinus bradycardia	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
<b>Ear and labyrinth disorders</b>	0 ( 0%)	0 ( 0%)	2 ( 16.7%)	2 ( 6.7%)
Hearing impaired	0 ( 0%)	0 ( 0%)	1 ( 8.3%)	1 ( 3.3%)
Tinnitus	0 ( 0%)	0 ( 0%)	1 ( 8.3%)	1 ( 3.3%)
<b>Endocrine disorders</b>	2 ( 33.3%)	4 ( 33.3%)	3 ( 25%)	9 ( 30%)
Hypothyroidism	2 ( 33.3%)	4 ( 33.3%)	2 ( 16.7%)	8 ( 26.7%)
Hyperparathyroidism	0 ( 0%)	0 ( 0%)	1 ( 8.3%)	1 ( 3.3%)
<b>Eye disorders</b>	0 ( 0%)	5 ( 41.7%)	2 ( 16.7%)	7 ( 23.3%)
Blurred vision	0 ( 0%)	1 ( 8.3%)	2 ( 16.7%)	3 ( 10%)
Cataract	0 ( 0%)	0 ( 0%)	1 ( 8.3%)	1 ( 3.3%)
Dry eye	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Eye pain	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Eyelid function disorder	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)

Retinal detachment	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Stye on left upper eyelid	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
<b>Gastrointestinal disorders</b>	5 ( 83.3%)	9 ( 75%)	6 ( 50%)	20 ( 66.7%)
Abdominal pain	3 ( 50%)	6 ( 50%)	2 ( 16.7%)	11 ( 36.7%)
Nausea	3 ( 50%)	3 ( 25%)	4 ( 33.3%)	10 ( 33.3%)
Constipation	3 ( 50%)	2 ( 16.7%)	4 ( 33.3%)	9 ( 30%)
Vomiting	0 ( 0%)	4 ( 33.3%)	4 ( 33.3%)	8 ( 26.7%)
Diarrhea	1 ( 16.7%)	1 ( 8.3%)	2 ( 16.7%)	4 ( 13.3%)
Bloating	3 ( 50%)	0 ( 0%)	0 ( 0%)	3 ( 10%)
Dry mouth	0 ( 0%)	2 ( 16.7%)	0 ( 0%)	2 ( 6.7%)
Flatulence	0 ( 0%)	1 ( 8.3%)	1 ( 8.3%)	2 ( 6.7%)
Abdominal distension	1 ( 16.7%)	0 ( 0%)	0 ( 0%)	1 ( 3.3%)
Gastroesophageal reflux disease	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Hemorrhoids	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Hernia umbilical	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
<b>General disorders and administration site conditions</b>	5 ( 83.3%)	11 ( 91.7%)	9 ( 75%)	25 ( 83.3%)
Fatigue	4 ( 66.7%)	9 ( 75%)	6 ( 50%)	19 ( 63.3%)
Pain	1 ( 16.7%)	4 ( 33.3%)	5 ( 41.7%)	10 ( 33.3%)
Fever	2 ( 33.3%)	3 ( 25%)	2 ( 16.7%)	7 ( 23.3%)
Edema limbs	4 ( 66.7%)	2 ( 16.7%)	0 ( 0%)	6 ( 20%)
Chills	1 ( 16.7%)	1 ( 8.3%)	1 ( 8.3%)	3 ( 10%)
Death NOS	0 ( 0%)	2 ( 16.7%)	0 ( 0%)	2 ( 6.7%)
Localized edema	0 ( 0%)	1 ( 8.3%)	1 ( 8.3%)	2 ( 6.7%)
Non-cardiac chest pain	0 ( 0%)	1 ( 8.3%)	1 ( 8.3%)	2 ( 6.7%)
Edema face	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Edema trunk	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)

Failure to Thrive	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Gait disturbance	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Malaise	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Metallic taste in mouth	0 ( 0.0%)	0 ( 0.0%)	1 ( 8.3%)	1 ( 3.3%)
Night Sweats	0 ( 0%)	1 ( 8.3%)	1 ( 8.3%)	2 ( 6.7%)
<b>Infections and infestations</b>	3 ( 50%)	6 ( 50%)	4 ( 33.3%)	13 ( 43.3%)
Upper respiratory infection	0 ( 0%)	4 ( 33.3%)	0 ( 0%)	4 ( 13.3%)
Urinary tract infection	1 ( 16.7%)	1 ( 8.3%)	1 ( 8.3%)	3 ( 10%)
Soft tissue infection	0 ( 0%)	0 ( 0%)	2 ( 16.7%)	2 ( 6.7%)
Lung infection	1 ( 16.7%)	0 ( 0%)	0 ( 0%)	1 ( 3.3%)
Rash pustular	0 ( 0%)	0 ( 0%)	1 ( 8.3%)	1 ( 3.3%)
Sinusitis	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Skin infection	1 ( 16.7%)	0 ( 0%)	0 ( 0%)	1 ( 3.3%)
<b>Injury, poisoning and procedural complications</b>	0 ( 0%)	3 ( 25%)	0 ( 0%)	3 ( 10%)
Fall	0 ( 0%)	2 ( 16.7%)	0 ( 0%)	2 ( 6.7%)
Tooth cracked	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
<b>Investigations</b>	6 ( 100%)	11 ( 91.7%)	10 ( 83.3%)	27 ( 90%)
Lymphocyte count decreased	5 ( 83.3%)	9 ( 75%)	3 ( 25%)	17 ( 56.7%)
CD4 lymphocytes decreased	3 ( 50%)	7 ( 58.3%)	3 ( 25%)	13 ( 43.3%)
Creatinine increased	3 ( 50%)	7 ( 58.3%)	3 ( 25%)	13 ( 43.3%)
Alkaline phosphatase increased	1 ( 16.7%)	6 ( 50%)	5 ( 41.7%)	12 ( 40%)
Aspartate aminotransferase increased	2 ( 33.3%)	4 ( 33.3%)	5 ( 41.7%)	11 ( 36.7%)
Alanine aminotransferase increased	1 ( 16.7%)	4 ( 33.3%)	5 ( 41.7%)	10 ( 33.3%)
White blood cell decreased	3 ( 50%)	4 ( 33.3%)	1 ( 8.3%)	8 ( 26.7%)
Platelet count decreased	1 ( 16.7%)	5 ( 41.7%)	1 ( 8.3%)	7 ( 23.3%)
Creatine Phosphokinase increased	0 ( 0%)	1 ( 8.3%)	5 ( 41.7%)	6 ( 20%)

Blood bilirubin increased	2 ( 33.3%)	2 ( 16.7%)	1 ( 8.3%)	5 ( 16.7%)
Neutrophil count decreased	2 ( 33.3%)	3 ( 25%)	0 ( 0%)	5 ( 16.7%)
Weight loss	1 ( 16.7%)	1 ( 8.3%)	2 ( 16.7%)	4 ( 13.3%)
INR increased	1 ( 16.7%)	0 ( 0%)	1 ( 8.3%)	2 ( 6.7%)
Activated partial thromboplastin time prolonged	1 ( 16.7%)	0 ( 0%)	0 ( 0%)	1 ( 3.3%)
Carbon Dioxide Decreased	0 ( 0%)	0 ( 0%)	1 ( 8.3%)	1 ( 3.3%)
Decreased RBC	0 ( 0%)	0 ( 0%)	1 ( 8.3%)	1 ( 3.3%)
Elevated Retic Count Percent	0 ( 0%)	0 ( 0%)	1 ( 8.3%)	1 ( 3.3%)
Increased CK	0 ( 0%)	0 ( 0.%)	1 ( 8.3%)	1 ( 3.3%)
Hyperphosphatemia	0 ( 0%)	0 ( 0.%)	1 ( 8.3%)	1 ( 3.3%)
Increased serum phosphorus	0 ( 0%)	0 ( 0%)	1 ( 8.3%)	1 ( 3.3%)
Parathyroid hormone abnormal	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
<b>Metabolism and nutrition disorders</b>	6 ( 100%)	12 ( 100%)	8 ( 66.7%)	26 ( 86.7%)
Hyponatremia	5 ( 83.3%)	5 ( 41.7%)	4 ( 33.3%)	14 ( 46.7%)
Anorexia	4 ( 66.7%)	3 ( 25%)	3 ( 25%)	10 ( 33.3%)
Hypoalbuminemia	2 ( 33.3%)	5 ( 41.7%)	2 ( 16.7%)	9 ( 30%)
Hypophosphatemia	1 ( 16.7%)	5 ( 41.7%)	3 ( 25%)	9 ( 30%)
Hypercalcemia	2 ( 33.3%)	4 ( 33.3%)	1 ( 8.3%)	7 ( 23.3%)
Hyperglycemia	1 ( 16.7%)	3 ( 25%)	2 ( 16.7%)	6 ( 20%)
Hypokalemia	3 ( 50%)	1 ( 8.3%)	2 ( 16.7%)	6 ( 20%)
Hypocalcemia	1 ( 16.7%)	1 ( 8.3%)	3 ( 25%)	5 ( 16.7%)
Hyperkalemia	0 ( 0%)	3 ( 25.0%)	1 ( 8.3%)	4 ( 13.3%)
Hypomagnesemia	0 ( 0%)	2 ( 16.7%)	1 ( 8.3%)	3 ( 10%)
Glucose intolerance	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Hypermagnesemia	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Hypernatremia	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)

Hypertriglyceridemia	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
<b>Musculoskeletal and connective tissue disorders</b>	3 ( 50%)	7 ( 58.3%)	7 ( 58.3%)	17 ( 56.7%)
Pain in extremity	2 ( 33.3%)	2 ( 16.7%)	4 ( 33.3%)	8 ( 26.7%)
Arthralgia	0 ( 0%)	2 ( 16.7%)	1 ( 8.3%)	3 ( 10%)
Back pain	0 ( 0%)	2 ( 16.7%)	1 ( 8.3%)	3 ( 10%)
Chest wall pain	0 ( 0%)	2 ( 16.7%)	0 ( 0%)	2 ( 6.7%)
Flank pain	0 ( 0%)	1 ( 8.3%)	1 ( 8.3%)	2 ( 6.7%)
Generalized muscle weakness	0 ( 0%)	1 ( 8.3%)	1 ( 8.3%)	2 ( 6.7%)
Myalgia	1 ( 16.7%)	1 ( 8.3%)	0 ( 0%)	2 ( 6.7%)
Bone pain	1 ( 16.7%)	0 ( 0%)	0 ( 0%)	1 ( 3.3%)
Joint range of motion decreased	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Joint stiffness	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Muscle weakness lower limb	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Neck pain	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Right hand stiffness	0 ( 0%)	2 ( 16.7%)	0 ( 0%)	2 ( 6.7%)
<b>Neoplasms benign, malignant and unspecified (incl cysts and polyps)</b>	2 ( 33.3%)	4 ( 33.3%)	1 ( 8.3%)	7 ( 23.3%)
Tumor pain	1 ( 16.7%)	0 ( 0%)	1 ( 8.3%)	2 ( 6.7%)
Prostate Cancer Progressive Disease	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Cyst behind left ear	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Death due to progressive disease	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Disease progression	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Metastatic anal carcinoma	1 ( 16.7%)	0 ( 0%)	0 ( 0%)	1 ( 3.3%)
<b>Nervous system disorders</b>	3 ( 50%)	5 ( 41.7%)	5 ( 41.7%)	13 ( 43.3%)
Headache	1 ( 16.7%)	2 ( 16.7%)	3 ( 25.0%)	6 ( 20%)
Peripheral sensory neuropathy	0 ( 0%)	3 ( 25%)	0 ( 0%)	3 ( 10%)

Dizziness	1 ( 16.7%)	0 ( 0%)	1 ( 8.3%)	2 ( 6.7%)
Tremor	0 ( 0%)	0 ( 0%)	2 ( 16.7%)	2 ( 6.7%)
Ataxia	1 ( 16.7%)	0 ( 0%)	0 ( 0%)	1 ( 3.3%)
Concentration impairment	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Dysarthria	1 ( 16.7%)	0 ( 0%)	0 ( 0%)	1 ( 3.3%)
Dysgeusia	0 ( 0%)	0 ( 0%)	1 ( 8.3%)	1 ( 3.3%)
Memory impairment	1 ( 16.7%)	0 ( 0%)	0 ( 0%)	1 ( 3.3%)
Paresthesia	0 ( 0%)	0 ( 0%)	1 ( 8.3%)	1 ( 3.3%)
<b>Psychiatric disorders</b>	<b>3 ( 50%)</b>	<b>4 ( 33.3%)</b>	<b>4 ( 33.3%)</b>	<b>11 ( 36.7%)</b>
Anxiety	2 ( 33.3%)	3 ( 25%)	2 ( 16.7%)	7 ( 23.3%)
Insomnia	2 ( 33.3%)	1 ( 8.3%)	2 ( 16.7%)	5 ( 16.7%)
Depression	0 ( 0%)	0 ( 0%)	2 ( 16.7%)	2 ( 6.7%)
Confusion	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
<b>Renal and urinary disorders</b>	<b>3 ( 50%)</b>	<b>3 ( 25%)</b>	<b>4 ( 33.3%)</b>	<b>10 ( 33.3%)</b>
Hematuria	1 ( 16.7%)	1 ( 8.3%)	1 ( 8.3%)	3 ( 10%)
Proteinuria	1 ( 16.7%)	1 ( 8.3%)	1 ( 8.3%)	3 ( 10%)
Urinary frequency	1 ( 16.7%)	1 ( 8.3%)	1 ( 8.3%)	3 ( 10%)
Acute kidney injury	1 ( 16.7%)	0 ( 0%)	1 ( 8.3%)	2 ( 6.7%)
Urinary retention	0 ( 0%)	1 ( 8.3%)	1 ( 8.3%)	2 ( 6.7%)
Urinary tract obstruction	1 ( 16.7%)	1 ( 8.3%)	0 ( 0%)	2 ( 6.7%)
Urinary urgency	1 ( 16.7%)	0 ( 0%)	1 ( 8.3%)	2 ( 6.7%)
Burning at urination	1 ( 16.7%)	0 ( 0%)	0 ( 0%)	1 ( 3.3%)
Dysuria	0 ( 0%)	0 ( 0%)	1 ( 8.3%)	1 ( 3.3%)
GFR Decreased	0 ( 0%)	0 ( 0%)	3 ( 25%)	2 ( 7%)
Hemoglobinuria	0 ( 0%)	0 ( 0%)	1 ( 8.3%)	1 ( 3.3%)
Penile condyloma	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)

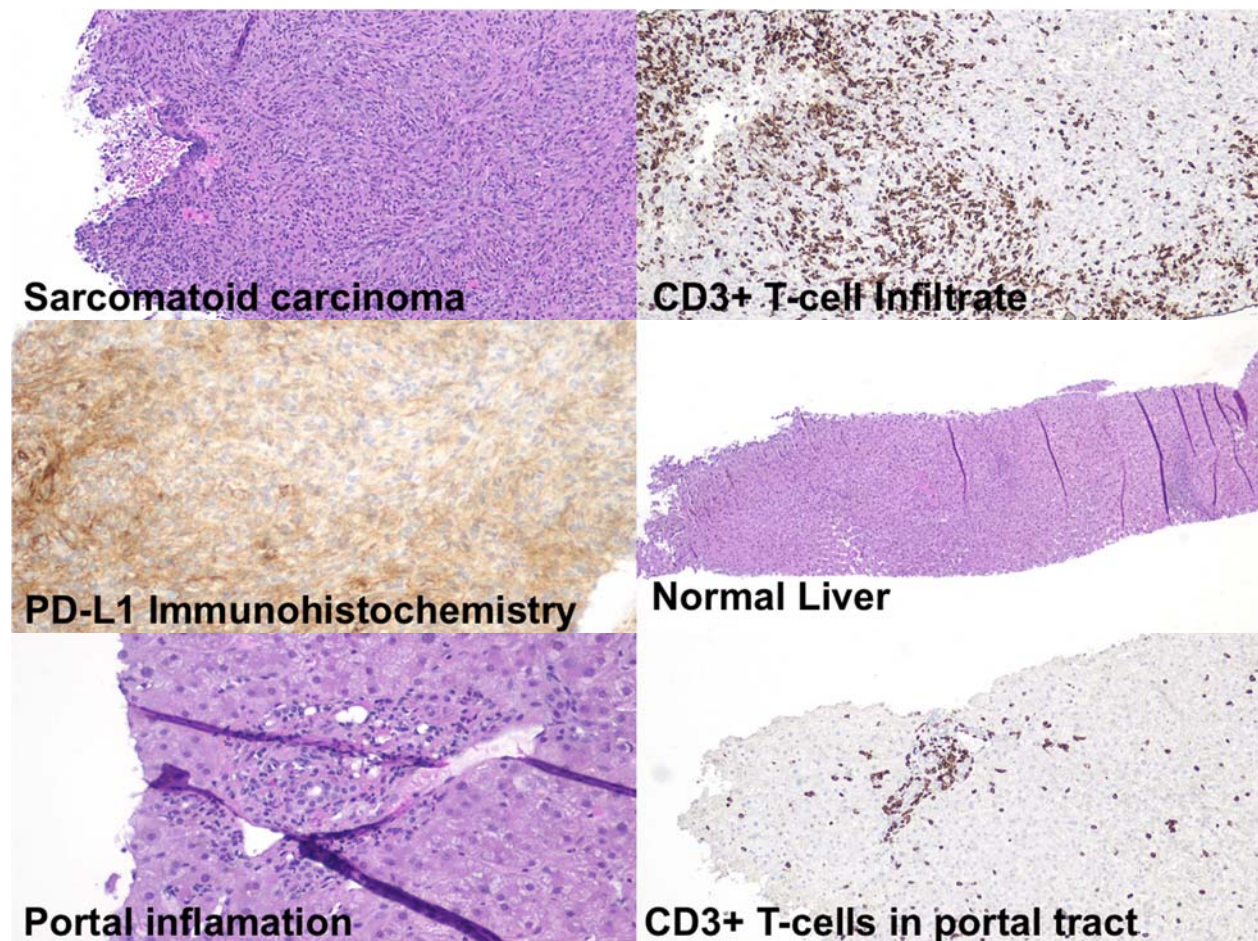
Urinary incontinence	0 ( 0%)	0 ( 0%)	1 ( 8.3%)	1 ( 3.3%)
<b>Reproductive system and breast disorders</b>	2 ( 33.3%)	1 ( 8.3%)	0 ( 0%)	3 ( 10%)
Genital edema	1 ( 16.7%)	1 ( 8.3%)	0 ( 0%)	2 ( 6.7%)
Pelvic pain	1 ( 16.7%)	0 ( 0%)	0 ( 0%)	1 ( 3.3%)
Scrotal pain	1 ( 16.7%)	0 ( 0%)	0 ( 0%)	1 ( 3.3%)
<b>Respiratory, thoracic and mediastinal disorders</b>	3 ( 50%)	10 ( 83.3%)	6 ( 50%)	19 ( 63.3%)
Dyspnea	2 ( 33.3%)	4 ( 33.3%)	4 ( 33.3%)	10 ( 33.3%)
Cough	0 ( 0%)	5 ( 41.7%)	2 ( 16.7%)	7 ( 23.3%)
Nasal congestion	0 ( 0%)	5 ( 41.7%)	2 ( 16.7%)	7 ( 23.3%)
Pneumonitis	1 ( 16.7%)	3 ( 25%)	0 ( 0%)	4 ( 13.3%)
Allergic rhinitis	0 ( 0%)	2 ( 16.7%)	0 ( 0%)	2 ( 6.7%)
Hiccups	1 ( 16.7%)	0 ( 0%)	1 ( 8.3%)	2 ( 6.7%)
Epistaxis	0 ( 0%)	0 ( 0%)	1 ( 8.3%)	1 ( 3.3%)
Pleural effusion	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Postnasal drip	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Productive cough	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Wheezing	1 ( 16.7%)	0 ( 0%)	0 ( 0%)	1 ( 3.3%)
Runny nose	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
<b>Skin and subcutaneous tissue disorders</b>	3 ( 50%)	6 ( 50%)	8 ( 66.7%)	17 ( 56.7%)
Pruritus	1 ( 16.7%)	1 ( 8.3%)	4 ( 33.3%)	6 ( 20%)
Dry skin	1 ( 16.7%)	3 ( 25%)	1 ( 8.3%)	5 ( 16.7%)
Hyperhidrosis	1 ( 16.7%)	2 ( 16.7%)	2 ( 16.7%)	5 ( 16.7%)
Rash maculo-papular	1 ( 16.7%)	1 ( 8.3%)	3 ( 25.0%)	5 ( 16.7%)
Alopecia	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Head nodule	1 ( 16.7%)	0 ( 0%)	0 ( 0%)	1 ( 3.3%)
Kaposi Sarcoma	0 ( 0%)	0 ( 0.0%)	1 ( 8.3%)	1 ( 3.3%)

Skin hypopigmentation	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Skin induration	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Skin ulceration	1 ( 16.7%)	0 ( 0%)	0 ( 0%)	1 ( 3.3%)
Xeroderma	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
Blister mouth	0 ( 0%)	0 ( 0%)	1 ( 8.3%)	1 ( 3.3%)
Night sweats	0 ( 0%)	1 ( 8.3%)	0 ( 0%)	1 ( 3.3%)
<b>Vascular disorders</b>	0 ( 0%)	2 ( 16.7%)	4 ( 33.3%)	6 ( 20%)
Hypotension	0 ( 0%)	2 ( 16.7%)	1 ( 8.3%)	3 ( 10%)
Hypertension	0 ( 0%)	0 ( 0%)	2 ( 16.7%)	2 ( 6.7%)
Thromboembolic event	0 ( 0%)	0 ( 0%)	1 ( 8.3%)	1 ( 3.3%)



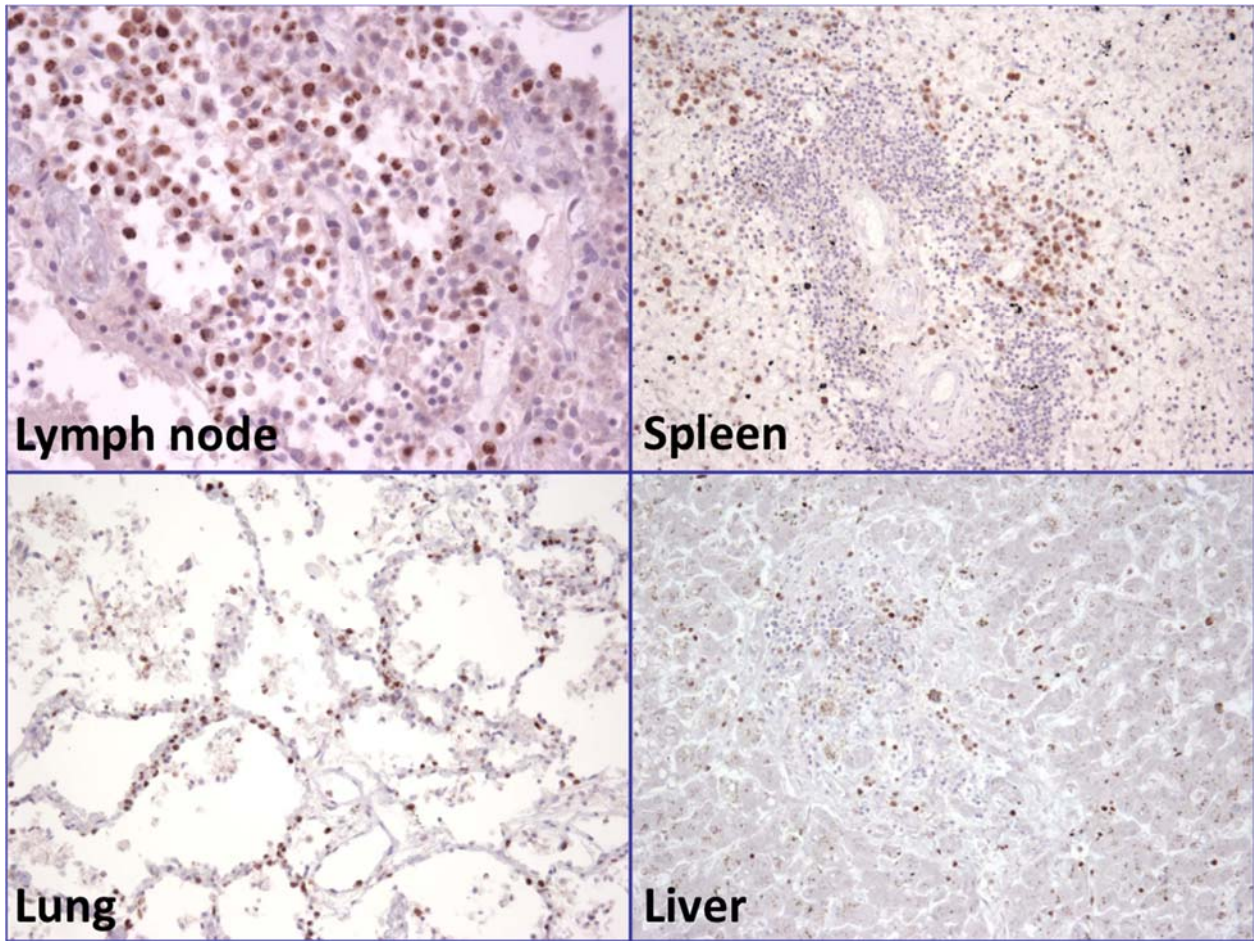
**eFigure 1. Liver biopsy in participant with sarcomatoid lung cancer with large metastases to liver who developed immune related AST/ALT after administration of pembrolizumab**

Results demonstrated viable tumor that was strongly PD-L1 positive and that had substantial T-cell infiltrates in the tumor with associated portal inflammation suggesting this event was related to immune response to the tumor in the setting of anti-PD-1 therapy. Participant was taken off therapy due to inability to titrate steroids.



**eFigure 2. Autopsy findings in participant who died of Kaposi sarcoma  
herpesvirus associated polyclonal B-cell lymphoproliferation**

A 61-year-old male participant who had been on ART for 22 years, and who had been treated for KS for 9 years received pembrolizumab on study. He had prior intermittent elevation of peripheral blood mononuclear cell-associated KSHV DNA and met working criteria for KSHV-associated inflammatory cytokine syndrome (KICS) 4 years prior to enrolling on the study. A work up at the time did not reveal KSHV-MCD and he was asymptomatic at the time of enrollment, but had an elevated peripheral blood mononuclear-cell associated KSHV viral load. After the second cycle of therapy, the patient developed thrombocytopenia, effusions, and edema originally managed with corticosteroids. Although initially stabilized, he subsequently developed acute worsening of symptoms with profound anemia and hyperbilirubinemia and anasarca at an outside hospital and died of respiratory distress. Autopsy was performed. Below: KSHV encoded latency-associated nuclear antigen (brown) highlighting KSHV infected cells in the lymph node, spleen, lung and liver. Immunoglobulin PCR revealed a polyclonal pattern in the spleen and effusions.



**eFigure 3. 18-fluorodeoxyglucose positron emission tomography in participant with chemotherapy-refractory primary effusion lymphoma demonstrating improvement after pembrolizumab**

The participant had resolution of lymphoma symptoms. Circulating KSHV viral load decreased from 6,275 copies/10<sup>6</sup> peripheral blood mononuclear cells to undetectable after 6 cycles of pembrolizumab

