

Supplementary Online Content

Kim RD, Chung V, Alese OB, et al. A phase 2 multi-institutional study of nivolumab for patients with advanced refractory biliary tract cancer. *JAMA Oncol*. Published online April 30, 2020. doi:10.1001/jamaoncol.2020.0930

eFigure 1. Waterfall Plot of Best Percentage Change in Tumor Lesion Size From Baseline and Spider Plot of Percentage Change in Tumor Lesion Size From Baseline Over Time by Investigator Assessment

eFigure 2. Kaplan-Meier Estimates of Duration of Response in Responders

eFigure 3. Kaplan-Meier Estimates of Progression-Free Survival and Overall Survival in Evaluable Patients

eFigure 4. Kaplan-Meier Estimates of Progression-Free Survival and Overall Survival by Failed Line of Systemic Therapy

eFigure 5. Representative Immunohistochemical Staining of PD-L1 and PD-1

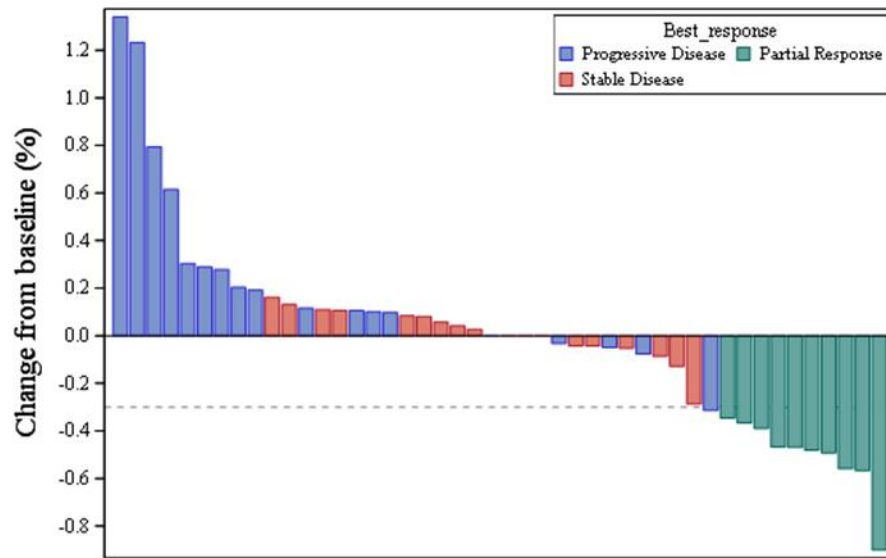
eFigure 6. Kaplan-Meier Estimates of Progression-Free Survival and Overall Survival by PD-L1 Expression Status (Cutoff >10%)

eTable 1. Patient Characteristics

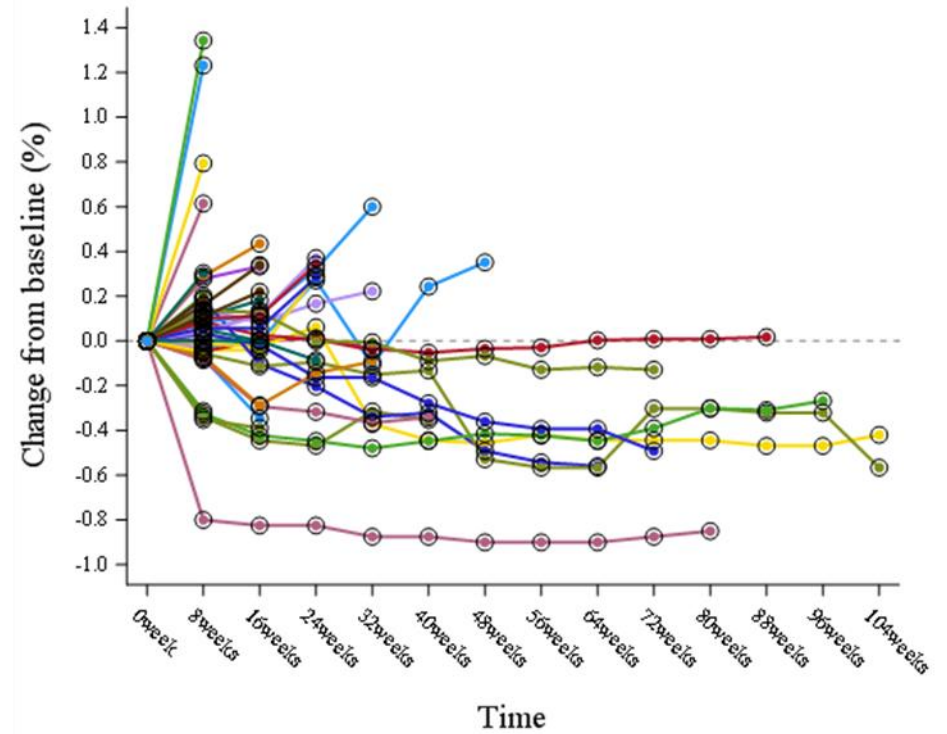
eTable 2. Treatment-Related Adverse Events

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

Waterfall Plot

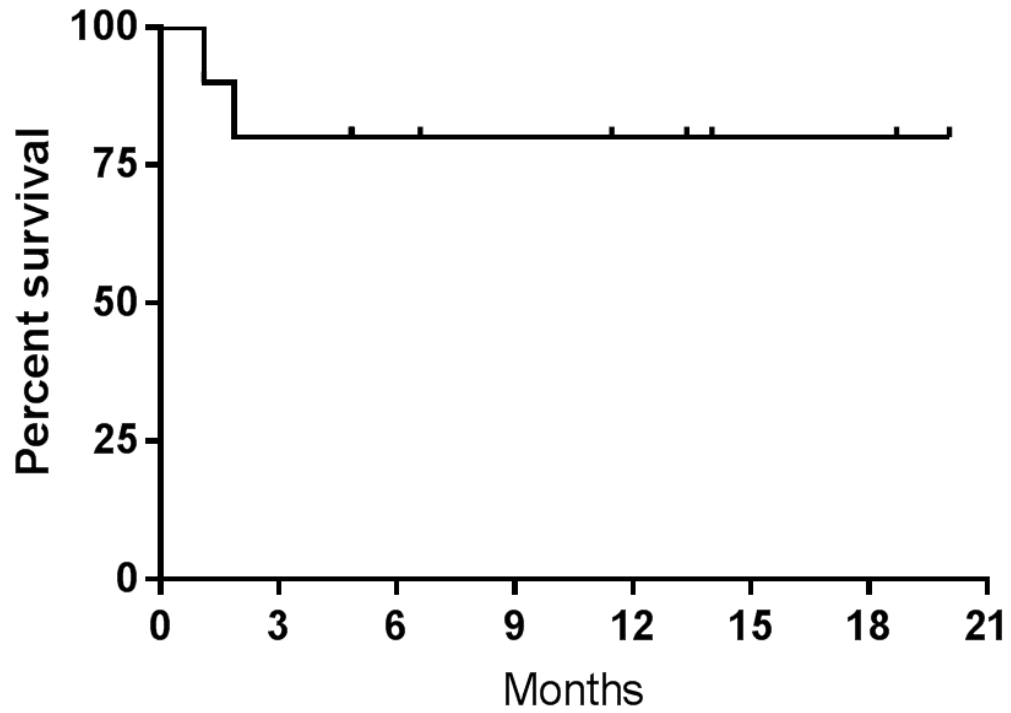


Spider Plot



eFigure 1. Waterfall Plot of Best Percentage Change in Tumor Lesion Size From Baseline and Spider Plot of Percentage Change in Tumor Lesion Size From Baseline Over Time by Investigator Assessment

Duration of Response

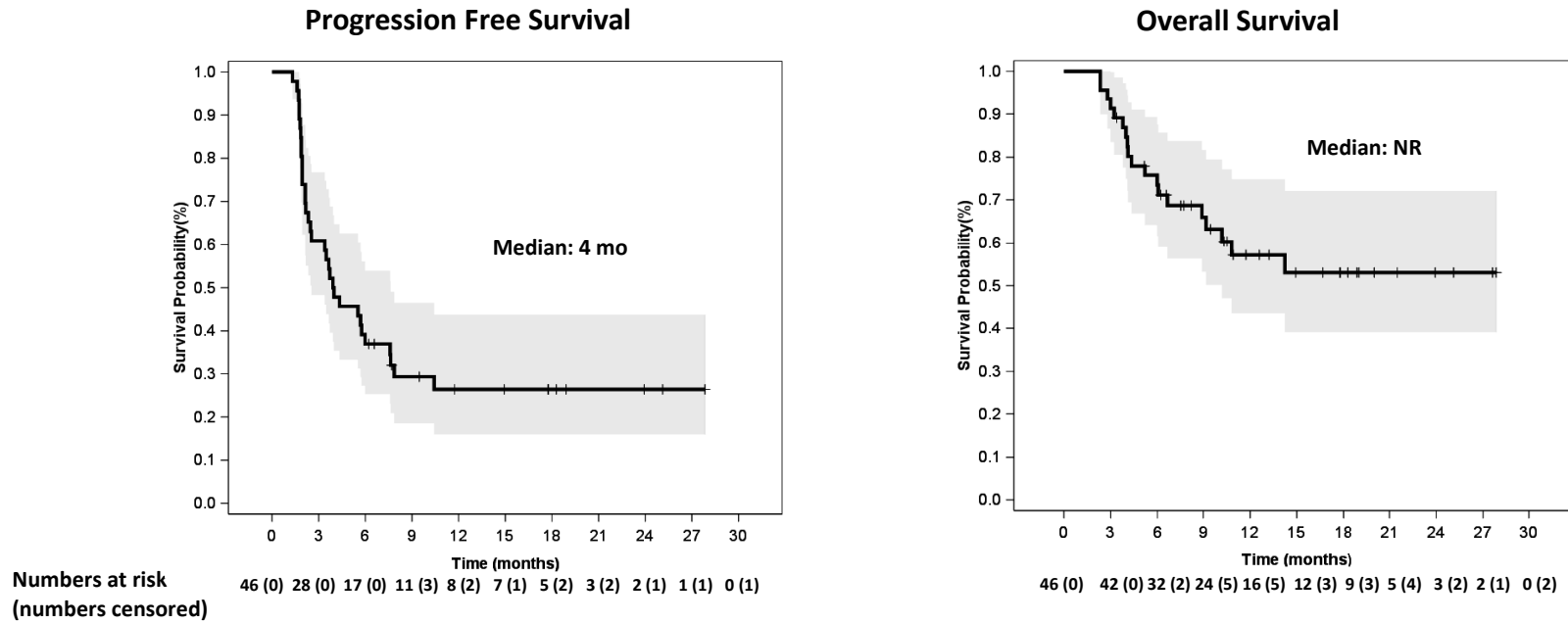


Numbers at risk
(numbers censored)

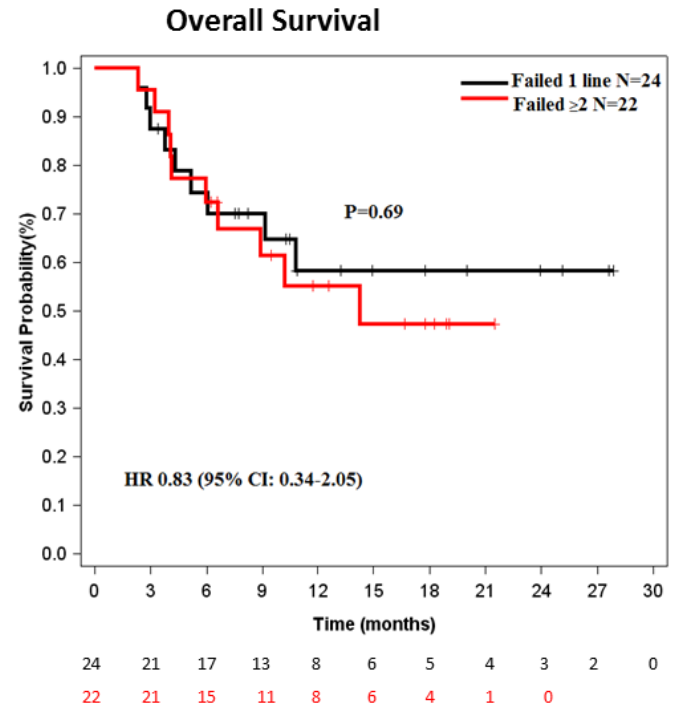
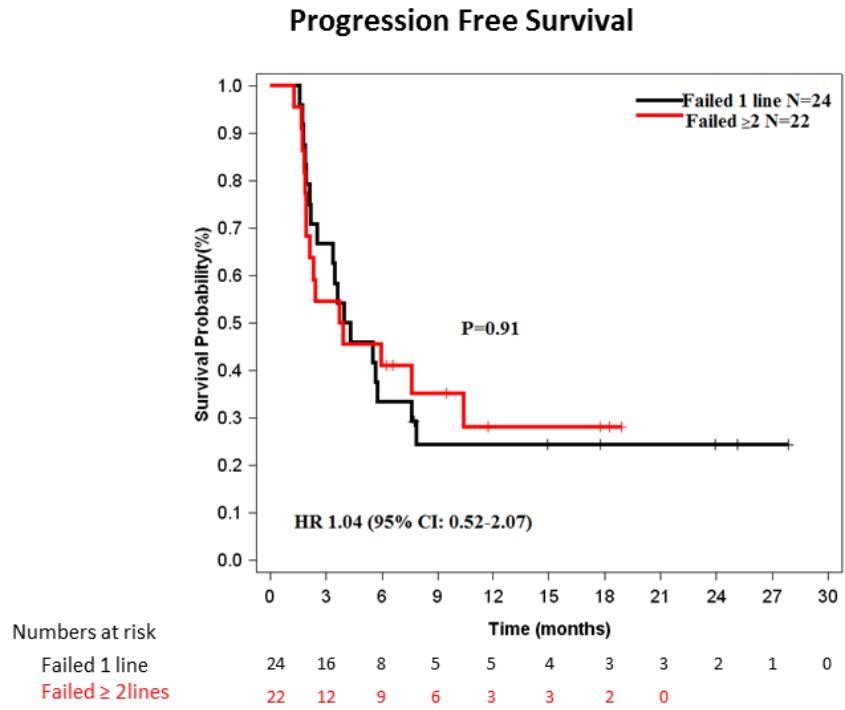
Months	0	3	6	9	12	15	18	21
Numbers at risk	10 (0)	9 (0)	7 (2)	6 (1)	5 (1)	3 (2)	3 (0)	1 (2)

eFigure 2. Kaplan-Meier Estimates of Duration of Response in Responders

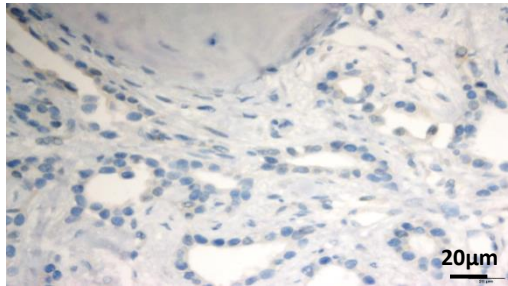
Evaluable patients (N=46)



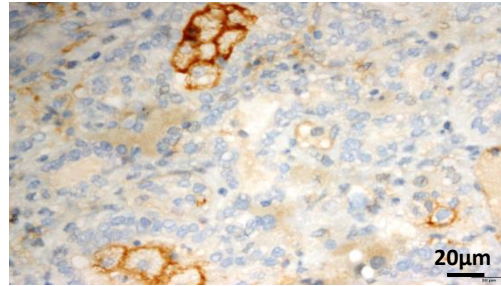
eFigure 3. Kaplan-Meier Estimates of Progression-Free Survival and Overall Survival in Evaluable Patients The shaded area represents the 95% confidence interval.



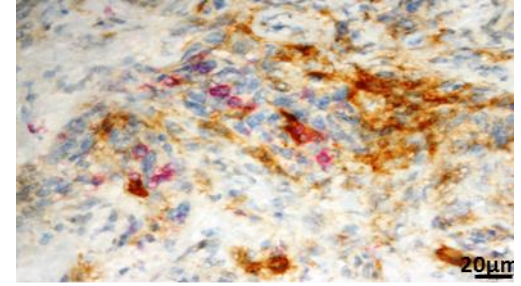
eFigure 4. Kaplan-Meier Estimates of Progression-Free Survival and Overall Survival by Failed Line of Systemic Therapy



Tumor PD-L1: negative
TIL PD-1: negative



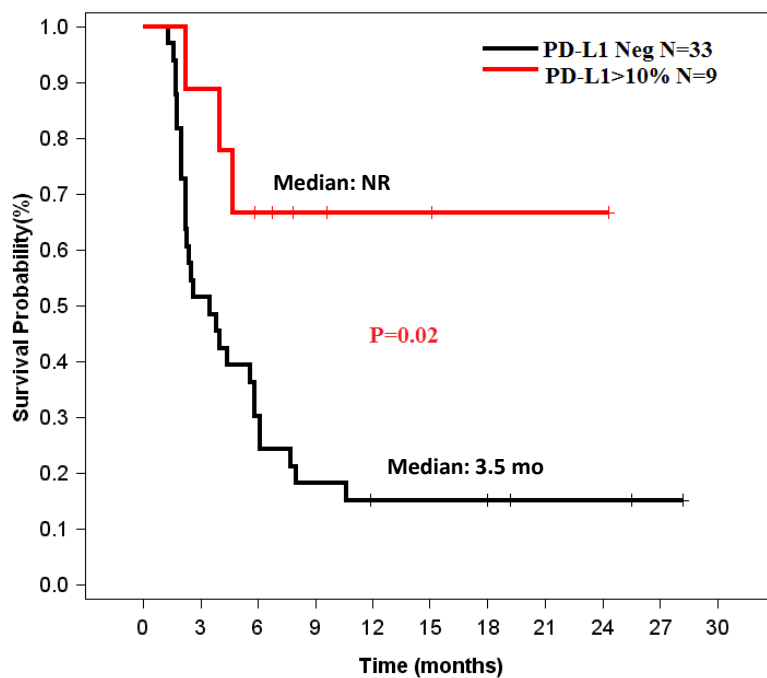
PD-L1: positive (brown)
PD-1: negative



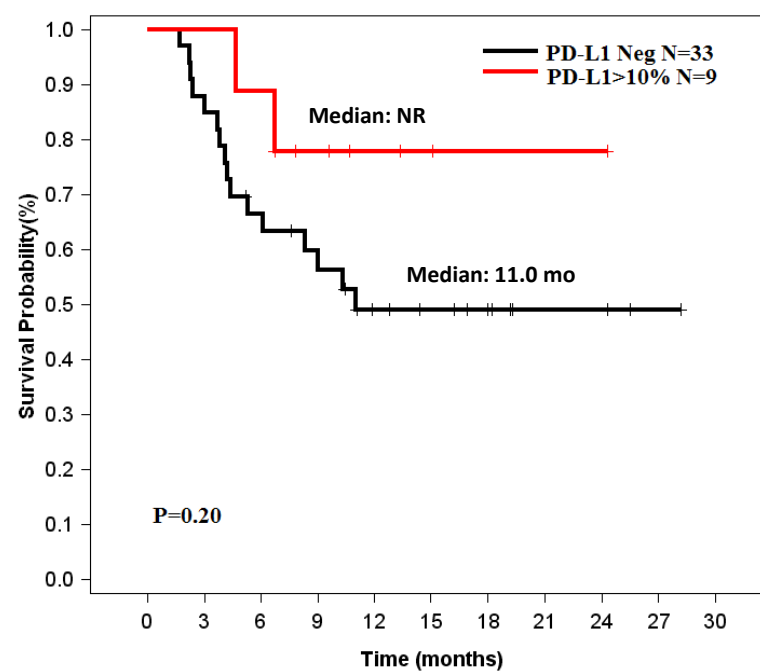
PD-L1: positive (brown)
PD-1: positive (red)

eFigure 5. Representative Immunohistochemical Staining of PD-L1 and PD-1

Progression Free Survival



Overall Survival



Numbers at risk	PD-L1 neg	33 (0)	17 (0)	10 (0)	6 (0)	4 (1)	4 (0)	4 (1)	2 (1)	2 (0)	1 (1)	0 (1)
(numbers censored)	PD-L1>10%	9 (0)	8 (0)	5 (1)	3 (2)	2 (1)	2 (0)	1 (1)	1 (0)	1 (0)	0 (1)	

33 (0)	29 (0)	21 (1)	17 (2)	11 (3)	9 (2)	7 (3)	3 (3)	3 (0)	1 (2)	0 (1)
9 (0)	9 (0)	8 (0)	5 (2)	3 (2)	2 (1)	1 (1)	1 (0)	1 (0)	0 (1)	

eFigure 6. Kaplan-Meier Estimates of Progression-Free Survival and Overall Survival by PD-L1 Expression Status (Cutoff >10%)

eTable 1. Patient Characteristics

Variable	N=54
Age	
median (range)	65 (28-86)
Gender	
Male	27 (50%)
Female	27 (50%)
Race	
White	35 (64.8%)
Hispanic	8 (14.8%)
African	8 (14.8%)
Asian	3 (5.6%)
ECOG PS	
0	18 (33.3%)
1	36 (66.7%)
Subtype	
Intrahepatic	32 (59.3%)
Extrahepatic	5 (9.3%)
Gallbladder	17 (31.5%)
Distant metastasis	
No (Locally advanced)	10 (18.5%)
Yes	44 (81.5%)
Previous Systemic treatment	
1st line	27 (50%)
2nd line +	27 (50%)

eTable 2. Treatment-Related Adverse Events

Toxicity	Grade (N=54)				Total
	1	2	3	4	
	<i>Number of patients with event (percent)</i>				
Alkaline phosphatase increased	6 (11.1)	5 (9.3)	2 (3.7)	0 (0)	13 (24.1)
Lymphocyte count decreased	10 (18.5)	1 (1.9)	1 (1.9)	0 (0)	12 (22.2)
Aspartate aminotransferase increased	10 (18.5)	1 (1.9)	0 (0)	0 (0)	11 (20.4)
Fatigue	5 (9.3)	5 (9.3)	1 (1.9)	0 (0)	11 (20.4)
Anemia	1 (1.9)	8 (14.8)	1 (1.9)	0 (0)	10 (18.5)
Alanine aminotransferase increased	7 (13.0)	2 (3.7)	0 (0)	0 (0)	9 (16.7)
Vomiting	9 (16.7)	0 (0)	0 (0)	0 (0)	9 (16.7)
Diarrhea	5 (9.3)	1 (1.9)	0 (0)	0 (0)	6 (11.1)
Nausea	4 (7.4)	2 (3.7)	0 (0)	0 (0)	6 (11.1)
Hyponatremia	1 (1.9)	0 (0)	3 (5.6)	0 (0)	4 (7.4)
Infusion related reaction	1 (1.9)	3 (5.6)	0 (0)	0 (0)	4 (7.4)
Pruritus	3 (5.6)	1 (1.9)	0 (0)	0 (0)	4 (7.4)
Rash maculo-papular	4 (7.4)	0 (0)	0 (0)	0 (0)	4 (7.4)
Blood bilirubin increased	1 (1.9)	1 (1.9)	1 (1.9)	0 (0)	3 (5.6)
Hypothyroidism	2 (3.7)	1 (1.9)	0 (0)	0 (0)	3 (5.6)
Platelet count decreased	3 (5.6)	0 (0)	0 (0)	0 (0)	3 (5.6)
Abdominal pain	1 (1.9)	0 (0)	1 (1.9)	0 (0)	2 (3.7)
Anorexia	2 (3.7)	0 (0)	0 (0)	0 (0)	2 (3.7)
Arthritis	2 (3.7)	0 (0)	0 (0)	0 (0)	2 (3.7)
Constipation	2 (3.7)	0 (0)	0 (0)	0 (0)	2 (3.7)
Dizziness	2 (3.7)	0 (0)	0 (0)	0 (0)	2 (3.7)
Hypercalcemia	1 (1.9)	1 (1.9)	0 (0)	0 (0)	2 (3.7)
Hyperglycemia	0 (0)	1 (1.9)	0 (0)	1 (1.9)	2 (3.7)
Hypertension	0 (0)	0 (0)	2 (3.7)	0 (0)	2 (3.7)
Skin and subcutaneous tissue disorders - Other, specify	2 (3.7)	0 (0)	0 (0)	0 (0)	2 (3.7)
Abdominal distension	1 (1.9)	0 (0)	0 (0)	0 (0)	1 (1.9)

Adrenal insufficiency	0 (0)	0 (0)	1 (1.9)	0 (0)	1 (1.9)
Allergic reaction	0 (0)	1 (1.9)	0 (0)	0 (0)	1 (1.9)
Arthralgia	1 (1.9)	0 (0)	0 (0)	0 (0)	1 (1.9)
Back pain	1 (1.9)	0 (0)	0 (0)	0 (0)	1 (1.9)
Blurred vision	1 (1.9)	0 (0)	0 (0)	0 (0)	1 (1.9)
Colitis	0 (0)	0 (0)	1 (1.9)	0 (0)	1 (1.9)
Dyspnea	1 (1.9)	0 (0)	0 (0)	0 (0)	1 (1.9)
Edema limbs	1 (1.9)	0 (0)	0 (0)	0 (0)	1 (1.9)
Electrocardiogram QT corrected interval prolonged	1 (1.9)	0 (0)	0 (0)	0 (0)	1 (1.9)
Endocrine disorders - Other, specify	1 (1.9)	0 (0)	0 (0)	0 (0)	1 (1.9)
Fever	0 (0)	1 (1.9)	0 (0)	0 (0)	1 (1.9)
Flushing	1 (1.9)	0 (0)	0 (0)	0 (0)	1 (1.9)
Gastrointestinal disorders - Other, specify	1 (1.9)	0 (0)	0 (0)	0 (0)	1 (1.9)
General disorders and administration site conditions - Other	1 (1.9)	0 (0)	0 (0)	0 (0)	1 (1.9)
Hyperkalemia	0 (0)	1 (1.9)	0 (0)	0 (0)	1 (1.9)
Hypermagnesemia	0 (0)	0 (0)	1 (1.9)	0 (0)	1 (1.9)
Hyperthyroidism	1 (1.9)	0 (0)	0 (0)	0 (0)	1 (1.9)
Hypoglycemia	1 (1.9)	0 (0)	0 (0)	0 (0)	1 (1.9)
Hypokalemia	0 (0)	0 (0)	0 (0)	1 (1.9)	1 (1.9)
Hypomagnesemia	1 (1.9)	0 (0)	0 (0)	0 (0)	1 (1.9)
Hypophosphatemia	0 (0)	1 (1.9)	0 (0)	0 (0)	1 (1.9)
INR increased	1 (1.9)	0 (0)	0 (0)	0 (0)	1 (1.9)
Malaise	0 (0)	1 (1.9)	0 (0)	0 (0)	1 (1.9)
Musculoskeletal and connective tissue disorder - Other, spe	1 (1.9)	0 (0)	0 (0)	0 (0)	1 (1.9)
Pain	1 (1.9)	0 (0)	0 (0)	0 (0)	1 (1.9)
Pneumonitis	1 (1.9)	0 (0)	0 (0)	0 (0)	1 (1.9)
Rash acneiform	1 (1.9)	0 (0)	0 (0)	0 (0)	1 (1.9)
Respiratory, thoracic and mediastinal disorders - Other, spe	1 (1.9)	0 (0)	0 (0)	0 (0)	1 (1.9)
Thromboembolic event	1 (1.9)	0 (0)	0 (0)	0 (0)	1 (1.9)
Thrombotic thrombocytopenic purpura	1 (1.9)	0 (0)	0 (0)	0 (0)	1 (1.9)

Weight gain	1 (1.9)	0 (0)	0 (0)	0 (0)	1 (1.9)
Weight loss	1 (1.9)	0 (0)	0 (0)	0 (0)	1 (1.9)
Total	108	38	14	2	162