Dossier zur Nutzenbewertung gemäß § 35a SGB V

Modul 4A

Anhang 4-G
AMNOG Analysen

Enfortumab vedotin (Padcev™)
Astellas Pharma GmbH

Perioperative Therapie bei erwachsenen Patienten mit resezierbarem muskelinvasivem Blasenkarzinom, die für eine Cisplatin-haltige Chemotherapie nicht infrage kommen; Kombination mit Pembrolizumab

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Patientencharakteristika

Table 303.1.1000.1: Summary of Disposition of Patients

	EV+Pembro	RC+PLND	Total
Number of Patients Enrolled			984
Randomized to Treatment			595
Discontinued Before Randomization to Treatment			389
Number of Randomized Patients (Stage 2)	170	174	344
SAF2 Analysis Set	167 (98.2%)	159 (91.4%)	326 (94.8%)
ITT2 Analysis Set	170 (100.0%)	174 (100.0%)	344 (100.0%)
Completed Treatment			
Yes	43 (25.3%)	149 (85.6%)	192 (55.8%)
No	127 (74.7%)	25 (14.4%)	152 (44.2%)
Overall Treatment Discontinuation			
Yes	116 (68.2%)	7 (4.0%)	123 (35.8%)
No	54 (31.8%)	167 (96.0%)	221 (64.2%)
Reason for Overall Treatment Discontinuation			
Adverse Event	59 (34.7%)	0	59 (17.2%)
Physician Decision	9 (5.3%)	0	9 (2.6%)
Progressive Disease	3 (1.8%)	0	3 (0.9%)
Relapse/Recurrence	12 (7.1%)	0	12 (3.5%)
Surgery Incomplete	2 (1.2%)	7 (4.0%)	9 (2.6%)
Withdrawal by Subject	31 (18.2%)	0	31 (9.0%)
Completed Study			
Yes	0	0	0
No	170 (100.0%)	174 (100.0%)	344 (100.0%)
Study Discontinuation			
Yes	40 (23.5%)	73 (42.0%)	113 (32.8%)
No	130 (76.5%)	101 (58.0%)	231 (67.2%)

Abbreviations: EV=enfortumab vedotin; Min=minimum; Max=maximum; n=number of patients with non-missing values; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; Q1=first quartile; Q3=third quartile; RC=radical cystectomy; SD=standard deviation.
(a) Time to last known alive date respective to data cutoff date is calculated as follows: (data cutoff date - last known alive date +1) / 30.4375.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.1: Summary of Disposition of Patients

	EV+Pembro	RC+PLND	Total
Reason for Study Discontinuation			
Death	37 (21.8%)	66 (37.9%)	103 (29.9%)
Withdrawal by Subject	3 (1.8%)	7 (4.0%)	10 (2.9%)
Time to Last Known Alive Date Respective to Data Cutoff Date (months) (a)			
n	170	174	344
Mean (SD)	5.5 (11.61)	9.5 (14.22)	7.5 (13.13)
Median	0.4	0.6	0.6
Q1 - Q3	0.1 - 0.7	0.3 - 16.5	0.2 - 9.4
Min - Max	0.0 - 48.8	0.0 - 51.3	0.0 - 51.3

Abbreviations: EV=enfortumab vedotin; Min=minimum; Max=maximum; n=number of patients with non-missing values; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; Q1=first quartile; Q3=third quartile; RC=radical cystectomy; SD=standard deviation.
(a) Time to last known alive date respective to data cutoff date is calculated as follows: (data cutoff date - last known alive date +1) / 30.4375.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.2: Summary of Baseline Demographics
ITT2 Analysis Set

Parameter and Category/Statistic	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Sex			
Male	137 (80.6%)	131 (75.3%)	268 (77.9%)
Female	33 (19.4%)	43 (24.7%)	76 (22.1%)
Age Group 1 (years)			
< 65	29 (17.1%)	29 (16.7%)	58 (16.9%)
>= 65	141 (82.9%)	145 (83.3%)	286 (83.1%)
Age Group 2 (years)			
< 65	29 (17.1%)	29 (16.7%)	58 (16.9%)
>= 65 and < 75	63 (37.1%)	77 (44.3%)	140 (40.7%)
>= 75 and < 85	74 (43.5%)	63 (36.2%)	137 (39.8%)
>= 85	4 (2.4%)	5 (2.9%)	9 (2.6%)
Age (years)			
n	170	174	344
Mean (SD)	72.1 (7.88)	71.6 (7.78)	71.8 (7.82)
Median	74.0	72.5	73.0
Q1 - Q3	67.0 - 78.0	67.0 - 77.0	67.0 - 77.0
Min - Max	47.0 - 87.0	46.0 - 87.0	46.0 - 87.0
Race			
American Indian or Alaska Native	0	1 (0.6%)	1 (0.3%)
Asian	31 (18.3%)	25 (14.6%)	56 (16.5%)
Black or African American	2 (1.2%)	2 (1.2%)	4 (1.2%)
Multiple	4 (2.4%)	7 (4.1%)	11 (3.2%)
White	132 (78.1%)	136 (79.5%)	268 (78.8%)
Missing	1	3	4

Abbreviations: CPS=combined positive score; CrCL=creatinine clearance; ECOG=eastern cooperative oncology group; EV=enfortumab vedotin; HbA1c=hemoglobin A1c; Min=minimum; Max=maximum; N=number of patients; n=number of patients with non-missing values; PD-L1=programmed cell death ligand 1; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; Q1=first quartile; Q3=third quartile; RC=radical cystectomy; SD=standard deviation.
(a) ECOG performance status assessed during screening.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.2: Summary of Baseline Demographics
ITT2 Analysis Set

Parameter and Category/Statistic	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Ethnicity			
Hispanic or Latino	8 (4.8%)	13 (7.8%)	21 (6.3%)
Not Hispanic or Latino	160 (95.2%)	153 (92.2%)	313 (93.7%)
Missing	2	8	10
Region			
United States	21 (12.4%)	23 (13.2%)	44 (12.8%)
European Union	78 (45.9%)	77 (44.3%)	155 (45.1%)
Most of World	71 (41.8%)	74 (42.5%)	145 (42.2%)
ECOG (a)			
0	102 (60.0%)	95 (54.6%)	197 (57.3%)
1	47 (27.6%)	53 (30.5%)	100 (29.1%)
2	21 (12.4%)	26 (14.9%)	47 (13.7%)
PD-L1 Expression in CPS >=10 (acc. to Stratification)			
CPS >= 10	80 (47.9%)	83 (48.0%)	163 (47.9%)
CPS < 10	87 (52.1%)	90 (52.0%)	177 (52.1%)
Missing	3	1	4
Cisplatin Status (Actual)			
Ineligible	142 (83.5%)	139 (79.9%)	281 (81.7%)
Eligible but Declined	28 (16.5%)	35 (20.1%)	63 (18.3%)
Cisplatin Status (Planned)			
Ineligible	140 (82.4%)	142 (81.6%)	282 (82.0%)
Eligible but Declined	30 (17.6%)	32 (18.4%)	62 (18.0%)

Abbreviations: CPS=combined positive score; CrCL=creatinine clearance; ECOG=eastern cooperative oncology group; EV=enfortumab vedotin; HbA1c=hemoglobin A1c; Min=minimum; Max=maximum; N=number of patients; n=number of patients with non-missing values; PD-L1=programmed cell death ligand 1; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; Q1=first quartile; Q3=third quartile; RC=radical cystectomy; SD=standard deviation.
(a) ECOG performance status assessed during screening.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.2: Summary of Baseline Demographics
ITT2 Analysis Set

Parameter and Category/Statistic	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Tumor Stage at Baseline (Actual)			
T2N0	30 (17.6%)	32 (18.4%)	62 (18.0%)
T3/T4aN0	133 (78.2%)	132 (75.9%)	265 (77.0%)
T1-4aN1	7 (4.1%)	10 (5.7%)	17 (4.9%)
Tumor Stage at Baseline (Planned)			
T2N0	31 (18.2%)	32 (18.4%)	63 (18.3%)
T3/T4aN0	132 (77.6%)	133 (76.4%)	265 (77.0%)
T1-4aN1	7 (4.1%)	9 (5.2%)	16 (4.7%)
Histology of Tumor			
Urothelial Carcinoma	152 (89.4%)	161 (92.5%)	313 (91.0%)
Urothelial Carcinoma with Glandular Differentiation	6 (3.5%)	3 (1.7%)	9 (2.6%)
Urothelial Carcinoma with Squamous Differentiation	9 (5.3%)	6 (3.4%)	15 (4.4%)
Urothelial Carcinoma with Variant Histology	3 (1.8%)	4 (2.3%)	7 (2.0%)
Smoking Status			
Never Smoker	55 (32.4%)	44 (25.3%)	99 (28.8%)
Former Smoker	82 (48.2%)	86 (49.4%)	168 (48.8%)
Current Smoker	33 (19.4%)	44 (25.3%)	77 (22.4%)
Weight Group (kg)			
<= 100	152 (89.4%)	168 (96.6%)	320 (93.0%)
> 100	18 (10.6%)	6 (3.4%)	24 (7.0%)
Weight (kg)			
n	170	174	344

Abbreviations: CPS=combined positive score; CrCL=creatinine clearance; ECOG=eastern cooperative oncology group; EV=enfortumab vedotin; HbA1c=hemoglobin A1c; Min=minimum; Max=maximum; N=number of patients; n=number of patients with non-missing values; PD-L1=programmed cell death ligand 1; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; Q1=first quartile; Q3=third quartile; RC=radical cystectomy; SD=standard deviation.
(a) ECOG performance status assessed during screening.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.2: Summary of Baseline Demographics
ITT2 Analysis Set

Parameter and Category/Statistic	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Mean (SD)	76.5 (18.08)	73.8 (15.64)	75.1 (16.91)
Median	75.0	72.0	73.7
Q1 - Q3	63.7 - 88.0	63.0 - 83.4	63.6 - 85.2
Min - Max	38.0 - 140.0	36.0 - 142.2	36.0 - 142.2
Body Mass Index Group (kg/m2)			
< 25	68 (40.0%)	79 (45.4%)	147 (42.7%)
25 to < 30	70 (41.2%)	62 (35.6%)	132 (38.4%)
>= 30	32 (18.8%)	33 (19.0%)	65 (18.9%)
Body Mass Index (kg/m2)			
n	170	174	344
Mean (SD)	25.9 (4.99)	25.7 (4.92)	25.8 (4.95)
Median	26.0	25.0	25.0
Q1 - Q3	23.0 - 29.0	23.0 - 28.0	23.0 - 28.0
Min - Max	14.0 - 47.0	15.0 - 46.0	14.0 - 47.0
Renal Function Based on CrCL (mL/min)			
>= 60	68 (40.0%)	72 (41.4%)	140 (40.7%)
>= 30 and < 60	102 (60.0%)	101 (58.0%)	203 (59.0%)
< 30	0	1 (0.6%)	1 (0.3%)
HbA1c Group (%)			
< 5.7	70 (42.2%)	79 (46.7%)	149 (44.5%)
>= 5.7 and < 6.5	68 (41.0%)	69 (40.8%)	137 (40.9%)
>= 6.5	28 (16.9%)	21 (12.4%)	49 (14.6%)
Missing	4	5	9

Abbreviations: CPS=combined positive score; CrCL=creatinine clearance; ECOG=eastern cooperative oncology group; EV=enfortumab vedotin; HbA1c=hemoglobin A1c; Min=minimum; Max=maximum; N=number of patients; n=number of patients with non-missing values; PD-L1=programmed cell death ligand 1; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; Q1=first quartile; Q3=third quartile; RC=radical cystectomy; SD=standard deviation.
(a) ECOG performance status assessed during screening.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.2: Summary of Baseline Demographics
ITT2 Analysis Set

Parameter and Category/Statistic	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
HbA1c (%)			
n	166	169	335
Mean (SD)	5.9 (0.70)	5.8 (0.61)	5.8 (0.66)
Median	5.8	5.7	5.7
Q1 - Q3	5.5 - 6.2	5.4 - 6.0	5.4 - 6.1
Min - Max	4.4 - 9.1	4.1 - 7.8	4.1 - 9.1
Time from Current Diagnosis to Randomization (days)			
n	170	174	344
Mean (SD)	61.4 (34.89)	58.9 (24.58)	60.1 (30.10)
Median	57.0	57.5	57.0
Q1 - Q3	43.0 - 73.0	43.0 - 72.0	43.0 - 73.0
Min - Max	12.0 - 407.0	1.0 - 203.0	1.0 - 407.0

Abbreviations: CPS=combined positive score; CrCL=creatinine clearance; ECOG=eastern cooperative oncology group; EV=enfortumab vedotin; HbA1c=hemoglobin A1c; Min=minimum; Max=maximum; N=number of patients; n=number of patients with non-missing values; PD-L1=programmed cell death ligand 1; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; Q1=first quartile; Q3=third quartile; RC=radical cystectomy; SD=standard deviation.
(a) ECOG performance status assessed during screening.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.3: Summary of Medical History by SOC/PT
ITT2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Overall	170 (100.0%)	174 (100.0%)	344 (100.0%)
Blood And Lymphatic System Disorders	32 (18.8%)	21 (12.1%)	53 (15.4%)
Anaemia	24 (14.1%)	16 (9.2%)	40 (11.6%)
Iron Deficiency Anaemia	2 (1.2%)	2 (1.1%)	4 (1.2%)
Lymphadenopathy	2 (1.2%)	0	2 (0.6%)
Thrombocytosis	1 (0.6%)	1 (0.6%)	2 (0.6%)
Abdominal Lymphadenopathy	1 (0.6%)	0	1 (0.3%)
Leukocytosis	0	1 (0.6%)	1 (0.3%)
Lymphoid Tissue Hyperplasia	0	1 (0.6%)	1 (0.3%)
Monocytosis	0	1 (0.6%)	1 (0.3%)
Normochromic Anaemia	0	1 (0.6%)	1 (0.3%)
Normocytic Anaemia	1 (0.6%)	0	1 (0.3%)
Retroperitoneal Lymphadenopathy	0	1 (0.6%)	1 (0.3%)
Splenic Vein Thrombosis	1 (0.6%)	0	1 (0.3%)
Splenomegaly	0	1 (0.6%)	1 (0.3%)
Thrombocytopenia	1 (0.6%)	0	1 (0.3%)
Thrombotic Thrombocytopenic Purpura	1 (0.6%)	0	1 (0.3%)
Cardiac Disorders	59 (34.7%)	64 (36.8%)	123 (35.8%)
Atrial Fibrillation	17 (10.0%)	12 (6.9%)	29 (8.4%)
Coronary Artery Disease	7 (4.1%)	17 (9.8%)	24 (7.0%)
Myocardial Ischaemia	12 (7.1%)	10 (5.7%)	22 (6.4%)
Arteriosclerosis Coronary Artery	8 (4.7%)	2 (1.1%)	10 (2.9%)
Cardiac Failure Chronic	4 (2.4%)	5 (2.9%)	9 (2.6%)
Myocardial Infarction	3 (1.8%)	5 (2.9%)	8 (2.3%)
Angina Pectoris	2 (1.2%)	5 (2.9%)	7 (2.0%)
Cardiac Failure	3 (1.8%)	4 (2.3%)	7 (2.0%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
SOCs are sorted alphabetically and PTs by descending patient count in the total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.3: Summary of Medical History by SOC/PT
ITT2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Acute Myocardial Infarction	4 (2.4%)	2 (1.1%)	6 (1.7%)
Arrhythmia	1 (0.6%)	5 (2.9%)	6 (1.7%)
Myocardial Fibrosis	2 (1.2%)	4 (2.3%)	6 (1.7%)
Bundle Branch Block Right	2 (1.2%)	3 (1.7%)	5 (1.5%)
Cardiomegaly	0	4 (2.3%)	4 (1.2%)
Hypertensive Heart Disease	2 (1.2%)	1 (0.6%)	3 (0.9%)
Pericardial Effusion	1 (0.6%)	2 (1.1%)	3 (0.9%)
Acute Coronary Syndrome	1 (0.6%)	1 (0.6%)	2 (0.6%)
Aortic Valve Incompetence	1 (0.6%)	1 (0.6%)	2 (0.6%)
Atrial Flutter	2 (1.2%)	0	2 (0.6%)
Atrioventricular Block	2 (1.2%)	0	2 (0.6%)
Bradycardia	0	2 (1.1%)	2 (0.6%)
Bundle Branch Block Left	0	2 (1.1%)	2 (0.6%)
Cardiac Failure Congestive	0	2 (1.1%)	2 (0.6%)
Defect Conduction Intraventricular	0	2 (1.1%)	2 (0.6%)
Ischaemic Cardiomyopathy	2 (1.2%)	0	2 (0.6%)
Sinus Bradycardia	1 (0.6%)	1 (0.6%)	2 (0.6%)
Tachycardia	1 (0.6%)	1 (0.6%)	2 (0.6%)
Angina Unstable	0	1 (0.6%)	1 (0.3%)
Aortic Valve Sclerosis	0	1 (0.6%)	1 (0.3%)
Arrhythmia Supraventricular	1 (0.6%)	0	1 (0.3%)
Atrioventricular Block First Degree	1 (0.6%)	0	1 (0.3%)
Cardiac Aneurysm	0	1 (0.6%)	1 (0.3%)
Cardiomyopathy	1 (0.6%)	0	1 (0.3%)
Coronary Artery Stenosis	1 (0.6%)	0	1 (0.3%)
Dilated Cardiomyopathy	0	1 (0.6%)	1 (0.3%)
Heart Failure With Reduced Ejection Fraction	1 (0.6%)	0	1 (0.3%)
Left Atrial Dilatation	0	1 (0.6%)	1 (0.3%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
SOCs are sorted alphabetically and PTs by descending patient count in the total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.3: Summary of Medical History by SOC/PT
ITT2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Left Ventricular Dysfunction	1 (0.6%)	0	1 (0.3%)
Left Ventricular Failure	0	1 (0.6%)	1 (0.3%)
Left Ventricular Hypertrophy	0	1 (0.6%)	1 (0.3%)
Mitral Valve Incompetence	0	1 (0.6%)	1 (0.3%)
Mitral Valve Sclerosis	0	1 (0.6%)	1 (0.3%)
Mitral Valve Stenosis	0	1 (0.6%)	1 (0.3%)
Pericarditis	1 (0.6%)	0	1 (0.3%)
Sinus Tachycardia	1 (0.6%)	0	1 (0.3%)
Supraventricular Extrasystoles	0	1 (0.6%)	1 (0.3%)
Tricuspid Valve Incompetence	0	1 (0.6%)	1 (0.3%)
Ventricular Arrhythmia	0	1 (0.6%)	1 (0.3%)
Ventricular Extrasystoles	0	1 (0.6%)	1 (0.3%)
Congenital, Familial And Genetic Disorders	9 (5.3%)	11 (6.3%)	20 (5.8%)
Corneal Dystrophy	1 (0.6%)	1 (0.6%)	2 (0.6%)
Dolichocolon	2 (1.2%)	0	2 (0.6%)
Hydrocele	0	2 (1.1%)	2 (0.6%)
Hypertrophic Cardiomyopathy	1 (0.6%)	1 (0.6%)	2 (0.6%)
Bicuspid Aortic Valve	0	1 (0.6%)	1 (0.3%)
Congenital Aortic Stenosis	0	1 (0.6%)	1 (0.3%)
Congenital Bladder Anomaly	0	1 (0.6%)	1 (0.3%)
Gene Mutation	1 (0.6%)	0	1 (0.3%)
Gilbert's Syndrome	1 (0.6%)	0	1 (0.3%)
Hypospadias	1 (0.6%)	0	1 (0.3%)
Optic Disc Pit	0	1 (0.6%)	1 (0.3%)
Phimosis	1 (0.6%)	0	1 (0.3%)
Renal Dysplasia	0	1 (0.6%)	1 (0.3%)
Renal Vessel Congenital Anomaly	1 (0.6%)	0	1 (0.3%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
SOCs are sorted alphabetically and PTs by descending patient count in the total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.3: Summary of Medical History by SOC/PT
ITT2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Spina Bifida	0	1 (0.6%)	1 (0.3%)
Tooth Agenesis	1 (0.6%)	0	1 (0.3%)
Type V Hyperlipidaemia	0	1 (0.6%)	1 (0.3%)
Ear And Labyrinth Disorders	38 (22.4%)	40 (23.0%)	78 (22.7%)
Deafness	19 (11.2%)	16 (9.2%)	35 (10.2%)
Hypoacusis	7 (4.1%)	9 (5.2%)	16 (4.7%)
Deafness Neurosensory	2 (1.2%)	6 (3.4%)	8 (2.3%)
Tinnitus	3 (1.8%)	3 (1.7%)	6 (1.7%)
Deafness Bilateral	3 (1.8%)	1 (0.6%)	4 (1.2%)
Deafness Unilateral	3 (1.8%)	1 (0.6%)	4 (1.2%)
Vertigo	2 (1.2%)	2 (1.1%)	4 (1.2%)
Ear Congestion	1 (0.6%)	1 (0.6%)	2 (0.6%)
Tympanic Membrane Perforation	1 (0.6%)	1 (0.6%)	2 (0.6%)
Cholesteatoma	0	1 (0.6%)	1 (0.3%)
Meniere's Disease	0	1 (0.6%)	1 (0.3%)
Presbyacusis	1 (0.6%)	0	1 (0.3%)
Vertigo Positional	0	1 (0.6%)	1 (0.3%)
Vestibular Ataxia	0	1 (0.6%)	1 (0.3%)
Endocrine Disorders	21 (12.4%)	23 (13.2%)	44 (12.8%)
Hypothyroidism	19 (11.2%)	17 (9.8%)	36 (10.5%)
Hyperthyroidism	1 (0.6%)	4 (2.3%)	5 (1.5%)
Goitre	1 (0.6%)	2 (1.1%)	3 (0.9%)
Thyroid Cyst	0	1 (0.6%)	1 (0.3%)
Eye Disorders	72 (42.4%)	59 (33.9%)	131 (38.1%)
Cataract	45 (26.5%)	36 (20.7%)	81 (23.5%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
SOCs are sorted alphabetically and PTs by descending patient count in the total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.3: Summary of Medical History by SOC/PT
ITT2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Presbyopia	6 (3.5%)	9 (5.2%)	15 (4.4%)
Glaucoma	3 (1.8%)	10 (5.7%)	13 (3.8%)
Dry Eye	7 (4.1%)	4 (2.3%)	11 (3.2%)
Age-Related Macular Degeneration	3 (1.8%)	4 (2.3%)	7 (2.0%)
Astigmatism	2 (1.2%)	4 (2.3%)	6 (1.7%)
Macular Degeneration	2 (1.2%)	3 (1.7%)	5 (1.5%)
Retinal Degeneration	2 (1.2%)	3 (1.7%)	5 (1.5%)
Arteriosclerotic Retinopathy	2 (1.2%)	2 (1.1%)	4 (1.2%)
Cataract Nuclear	3 (1.8%)	1 (0.6%)	4 (1.2%)
Epiretinal Membrane	3 (1.8%)	1 (0.6%)	4 (1.2%)
Hypermetropia	2 (1.2%)	2 (1.1%)	4 (1.2%)
Pterygium	3 (1.8%)	1 (0.6%)	4 (1.2%)
Retinopathy Hypertensive	3 (1.8%)	1 (0.6%)	4 (1.2%)
Vitreous Detachment	2 (1.2%)	2 (1.1%)	4 (1.2%)
Myopia	3 (1.8%)	0	3 (0.9%)
Arcus Lipoides	2 (1.2%)	0	2 (0.6%)
Corneal Opacity	0	2 (1.1%)	2 (0.6%)
Dermatochalasis	1 (0.6%)	1 (0.6%)	2 (0.6%)
Dry Age-Related Macular Degeneration	0	2 (1.1%)	2 (0.6%)
Meibomian Gland Dysfunction	1 (0.6%)	1 (0.6%)	2 (0.6%)
Normal Tension Glaucoma	1 (0.6%)	1 (0.6%)	2 (0.6%)
Optic Atrophy	0	2 (1.1%)	2 (0.6%)
Pinguecula	1 (0.6%)	1 (0.6%)	2 (0.6%)
Pseudophakia	1 (0.6%)	1 (0.6%)	2 (0.6%)
Punctate Keratitis	2 (1.2%)	0	2 (0.6%)
Retinal Drusen	1 (0.6%)	1 (0.6%)	2 (0.6%)
Retinal Tear	1 (0.6%)	1 (0.6%)	2 (0.6%)
Retinopathy	0	2 (1.1%)	2 (0.6%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
SOCs are sorted alphabetically and PTs by descending patient count in the total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.3: Summary of Medical History by SOC/PT
ITT2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Angle Closure Glaucoma	1 (0.6%)	0	1 (0.3%)
Aphakia	0	1 (0.6%)	1 (0.3%)
Atrophy Of Globe	0	1 (0.6%)	1 (0.3%)
Blindness Unilateral	0	1 (0.6%)	1 (0.3%)
Chalazion	0	1 (0.6%)	1 (0.3%)
Chorioretinal Disorder	1 (0.6%)	0	1 (0.3%)
Choroidal Rupture	0	1 (0.6%)	1 (0.3%)
Corneal Degeneration	1 (0.6%)	0	1 (0.3%)
Corneal Epithelial Wrinkling	0	1 (0.6%)	1 (0.3%)
Corneal Leukoma	0	1 (0.6%)	1 (0.3%)
Corneal Scar	0	1 (0.6%)	1 (0.3%)
Diabetic Retinal Oedema	0	1 (0.6%)	1 (0.3%)
Diabetic Retinopathy	1 (0.6%)	0	1 (0.3%)
Exfoliation Syndrome	1 (0.6%)	0	1 (0.3%)
Extraocular Muscle Disorder	1 (0.6%)	0	1 (0.3%)
Eye Disorder	1 (0.6%)	0	1 (0.3%)
Eye Inflammation	1 (0.6%)	0	1 (0.3%)
Eye Oedema	1 (0.6%)	0	1 (0.3%)
Eyelid Ptosis	1 (0.6%)	0	1 (0.3%)
Fuchs' Syndrome	1 (0.6%)	0	1 (0.3%)
Glaucomatous Optic Neuropathy	1 (0.6%)	0	1 (0.3%)
Hyalosis Asteroid	1 (0.6%)	0	1 (0.3%)
Keratopathy	1 (0.6%)	0	1 (0.3%)
Macular Hole	1 (0.6%)	0	1 (0.3%)
Maculopathy	1 (0.6%)	0	1 (0.3%)
Mydriasis	0	1 (0.6%)	1 (0.3%)
Myopic Chorioretinal Degeneration	0	1 (0.6%)	1 (0.3%)
Narrow Anterior Chamber Angle	0	1 (0.6%)	1 (0.3%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
SOCs are sorted alphabetically and PTs by descending patient count in the total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.3: Summary of Medical History by SOC/PT
ITT2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Neovascular Age-Related Macular Degeneration	1 (0.6%)	0	1 (0.3%)
Optic Disc Telangiectasia	0	1 (0.6%)	1 (0.3%)
Optic Ischaemic Neuropathy	0	1 (0.6%)	1 (0.3%)
Optic Nerve Cupping	0	1 (0.6%)	1 (0.3%)
Posterior Capsule Opacification	0	1 (0.6%)	1 (0.3%)
Refraction Disorder	1 (0.6%)	0	1 (0.3%)
Retinal Detachment	0	1 (0.6%)	1 (0.3%)
Retinal Dystrophy	1 (0.6%)	0	1 (0.3%)
Retinal Exudates	0	1 (0.6%)	1 (0.3%)
Retinal Vascular Disorder	0	1 (0.6%)	1 (0.3%)
Retinal Vasculitis	1 (0.6%)	0	1 (0.3%)
Retinal Vein Occlusion	1 (0.6%)	0	1 (0.3%)
Retinoschisis	1 (0.6%)	0	1 (0.3%)
Strabismus	0	1 (0.6%)	1 (0.3%)
Visual Impairment	1 (0.6%)	0	1 (0.3%)
Vitreous Disorder	1 (0.6%)	0	1 (0.3%)
Vitreous Opacities	1 (0.6%)	0	1 (0.3%)
Gastrointestinal Disorders	68 (40.0%)	56 (32.2%)	124 (36.0%)
Constipation	19 (11.2%)	15 (8.6%)	34 (9.9%)
Gastrooesophageal Reflux Disease	12 (7.1%)	8 (4.6%)	20 (5.8%)
Diverticulum Intestinal	9 (5.3%)	10 (5.7%)	19 (5.5%)
Inguinal Hernia	9 (5.3%)	4 (2.3%)	13 (3.8%)
Large Intestine Polyp	7 (4.1%)	5 (2.9%)	12 (3.5%)
Haemorrhoids	5 (2.9%)	4 (2.3%)	9 (2.6%)
Umbilical Hernia	5 (2.9%)	3 (1.7%)	8 (2.3%)
Hiatus Hernia	1 (0.6%)	5 (2.9%)	6 (1.7%)
Pancreatitis Chronic	2 (1.2%)	4 (2.3%)	6 (1.7%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
SOCs are sorted alphabetically and PTs by descending patient count in the total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.3: Summary of Medical History by SOC/PT
ITT2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Abdominal Pain	3 (1.8%)	2 (1.1%)	5 (1.5%)
Diarrhoea	5 (2.9%)	0	5 (1.5%)
Dyspepsia	2 (1.2%)	3 (1.7%)	5 (1.5%)
Gastric Ulcer	3 (1.8%)	2 (1.1%)	5 (1.5%)
Chronic Gastritis	1 (0.6%)	3 (1.7%)	4 (1.2%)
Gastritis	1 (0.6%)	3 (1.7%)	4 (1.2%)
Diverticulum	2 (1.2%)	1 (0.6%)	3 (0.9%)
Nausea	1 (0.6%)	2 (1.1%)	3 (0.9%)
Abdominal Pain Lower	2 (1.2%)	0	2 (0.6%)
Colitis Ulcerative	1 (0.6%)	1 (0.6%)	2 (0.6%)
Dental Caries	1 (0.6%)	1 (0.6%)	2 (0.6%)
Duodenal Ulcer	1 (0.6%)	1 (0.6%)	2 (0.6%)
Intestinal Polyp	0	2 (1.1%)	2 (0.6%)
Mesenteric Panniculitis	1 (0.6%)	1 (0.6%)	2 (0.6%)
Oesophagitis	2 (1.2%)	0	2 (0.6%)
Peptic Ulcer	2 (1.2%)	0	2 (0.6%)
Abdominal Discomfort	1 (0.6%)	0	1 (0.3%)
Abdominal Hernia	1 (0.6%)	0	1 (0.3%)
Anal Fissure	1 (0.6%)	0	1 (0.3%)
Ascites	1 (0.6%)	0	1 (0.3%)
Colitis	0	1 (0.6%)	1 (0.3%)
Dry Mouth	1 (0.6%)	0	1 (0.3%)
Duodenal Polyp	0	1 (0.6%)	1 (0.3%)
Duodenitis	0	1 (0.6%)	1 (0.3%)
Dysphagia	1 (0.6%)	0	1 (0.3%)
Eructation	0	1 (0.6%)	1 (0.3%)
Gastric Polyps	0	1 (0.6%)	1 (0.3%)
Gastritis Erosive	0	1 (0.6%)	1 (0.3%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
SOCs are sorted alphabetically and PTs by descending patient count in the total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.3: Summary of Medical History by SOC/PT
ITT2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Gastrointestinal Angiodysplasia	1 (0.6%)	0	1 (0.3%)
Intussusception	1 (0.6%)	0	1 (0.3%)
Irritable Bowel Syndrome	1 (0.6%)	0	1 (0.3%)
Oesophageal Achalasia	0	1 (0.6%)	1 (0.3%)
Oesophagitis Ulcerative	1 (0.6%)	0	1 (0.3%)
Pancreatic Duct Dilatation	0	1 (0.6%)	1 (0.3%)
Rectal Tenesmus	1 (0.6%)	0	1 (0.3%)
Salivary Hypersecretion	1 (0.6%)	0	1 (0.3%)
Small Intestinal Obstruction	1 (0.6%)	0	1 (0.3%)
Tooth Impacted	0	1 (0.6%)	1 (0.3%)
Tooth Loss	1 (0.6%)	0	1 (0.3%)
Varices Oesophageal	0	1 (0.6%)	1 (0.3%)
Vomiting	1 (0.6%)	0	1 (0.3%)
General Disorders And Administration Site Conditions	24 (14.1%)	11 (6.3%)	35 (10.2%)
Fatigue	15 (8.8%)	6 (3.4%)	21 (6.1%)
Oedema Peripheral	5 (2.9%)	2 (1.1%)	7 (2.0%)
Pain	3 (1.8%)	3 (1.7%)	6 (1.7%)
Asthenia	3 (1.8%)	0	3 (0.9%)
Chest Pain	1 (0.6%)	1 (0.6%)	2 (0.6%)
Gait Disturbance	2 (1.2%)	0	2 (0.6%)
Catheter Site Pain	0	1 (0.6%)	1 (0.3%)
Chills	0	1 (0.6%)	1 (0.3%)
Cyst	1 (0.6%)	0	1 (0.3%)
Generalised Oedema	0	1 (0.6%)	1 (0.3%)
Hernia	0	1 (0.6%)	1 (0.3%)
Medical Device Pain	1 (0.6%)	0	1 (0.3%)
Pyrexia	0	1 (0.6%)	1 (0.3%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
SOCs are sorted alphabetically and PTs by descending patient count in the total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.3: Summary of Medical History by SOC/PT
ITT2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Suprapubic Pain	1 (0.6%)	0	1 (0.3%)
Hepatobiliary Disorders	20 (11.8%)	25 (14.4%)	45 (13.1%)
Cholelithiasis	7 (4.1%)	10 (5.7%)	17 (4.9%)
Hepatic Cyst	6 (3.5%)	9 (5.2%)	15 (4.4%)
Hepatic Steatosis	5 (2.9%)	0	5 (1.5%)
Cholecystitis Chronic	0	2 (1.1%)	2 (0.6%)
Gallbladder Polyp	0	2 (1.1%)	2 (0.6%)
Hepatomegaly	1 (0.6%)	1 (0.6%)	2 (0.6%)
Liver Disorder	0	2 (1.1%)	2 (0.6%)
Bile Duct Stenosis	1 (0.6%)	0	1 (0.3%)
Biliary Dilatation	0	1 (0.6%)	1 (0.3%)
Cholecystitis	1 (0.6%)	0	1 (0.3%)
Dilatation Intrahepatic Duct Acquired	0	1 (0.6%)	1 (0.3%)
Hepatitis	1 (0.6%)	0	1 (0.3%)
Hepatitis Cholestatic	1 (0.6%)	0	1 (0.3%)
Metabolic Dysfunction-Associated Liver Disease	0	1 (0.6%)	1 (0.3%)
Porcelain Gallbladder	1 (0.6%)	0	1 (0.3%)
Post Cholecystectomy Syndrome	1 (0.6%)	0	1 (0.3%)
Immune System Disorders	10 (5.9%)	12 (6.9%)	22 (6.4%)
Drug Hypersensitivity	7 (4.1%)	2 (1.1%)	9 (2.6%)
Seasonal Allergy	1 (0.6%)	6 (3.4%)	7 (2.0%)
Contrast Media Allergy	3 (1.8%)	2 (1.1%)	5 (1.5%)
Allergy To Metals	1 (0.6%)	0	1 (0.3%)
Contrast Media Reaction	0	1 (0.6%)	1 (0.3%)
Food Allergy	0	1 (0.6%)	1 (0.3%)
Hypersensitivity	0	1 (0.6%)	1 (0.3%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
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ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.3: Summary of Medical History by SOC/PT
ITT2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Infections And Infestations	43 (25.3%)	32 (18.4%)	75 (21.8%)
Urinary Tract Infection	8 (4.7%)	10 (5.7%)	18 (5.2%)
Covid-19	8 (4.7%)	4 (2.3%)	12 (3.5%)
Cystitis	4 (2.4%)	2 (1.1%)	6 (1.7%)
Pneumonia	3 (1.8%)	2 (1.1%)	5 (1.5%)
Pyelonephritis Chronic	2 (1.2%)	3 (1.7%)	5 (1.5%)
Diverticulitis	1 (0.6%)	2 (1.1%)	3 (0.9%)
Escherichia Urinary Tract Infection	2 (1.2%)	1 (0.6%)	3 (0.9%)
Peritonitis	0	3 (1.7%)	3 (0.9%)
Rhinitis	2 (1.2%)	1 (0.6%)	3 (0.9%)
Appendicitis	1 (0.6%)	1 (0.6%)	2 (0.6%)
Chronic Sinusitis	1 (0.6%)	1 (0.6%)	2 (0.6%)
Fungal Infection	2 (1.2%)	0	2 (0.6%)
Helicobacter Gastritis	2 (1.2%)	0	2 (0.6%)
Hepatitis A	1 (0.6%)	1 (0.6%)	2 (0.6%)
Herpes Zoster	1 (0.6%)	1 (0.6%)	2 (0.6%)
Pulmonary Tuberculosis	0	2 (1.1%)	2 (0.6%)
Tonsillitis	1 (0.6%)	1 (0.6%)	2 (0.6%)
Tuberculosis	1 (0.6%)	1 (0.6%)	2 (0.6%)
Adenoiditis	1 (0.6%)	0	1 (0.3%)
Asymptomatic Bacteriuria	0	1 (0.6%)	1 (0.3%)
Bacterial Sepsis	1 (0.6%)	0	1 (0.3%)
Campylobacter Infection	1 (0.6%)	0	1 (0.3%)
Chronic Tonsillitis	1 (0.6%)	0	1 (0.3%)
Conjunctivitis	1 (0.6%)	0	1 (0.3%)
Coronavirus Infection	0	1 (0.6%)	1 (0.3%)
Covid-19 Pneumonia	0	1 (0.6%)	1 (0.3%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
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ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.3: Summary of Medical History by SOC/PT
ITT2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Device Related Infection	1 (0.6%)	0	1 (0.3%)
Ear Infection	1 (0.6%)	0	1 (0.3%)
Encephalitis	1 (0.6%)	0	1 (0.3%)
Epididymitis	1 (0.6%)	0	1 (0.3%)
Genital Candidiasis	1 (0.6%)	0	1 (0.3%)
Helicobacter Infection	0	1 (0.6%)	1 (0.3%)
Herpes Simplex	1 (0.6%)	0	1 (0.3%)
Human Polyomavirus Infection	1 (0.6%)	0	1 (0.3%)
Influenza	0	1 (0.6%)	1 (0.3%)
Laryngitis	0	1 (0.6%)	1 (0.3%)
Lower Respiratory Tract Infection	0	1 (0.6%)	1 (0.3%)
Morganella Infection	1 (0.6%)	0	1 (0.3%)
Onychomycosis	0	1 (0.6%)	1 (0.3%)
Oral Herpes	1 (0.6%)	0	1 (0.3%)
Otitis Externa	0	1 (0.6%)	1 (0.3%)
Otitis Media Chronic	1 (0.6%)	0	1 (0.3%)
Pneumonia Influenzal	0	1 (0.6%)	1 (0.3%)
Pneumonia Necrotising	0	1 (0.6%)	1 (0.3%)
Proteus Infection	0	1 (0.6%)	1 (0.3%)
Pseudomembranous Colitis	0	1 (0.6%)	1 (0.3%)
Pyelitis	0	1 (0.6%)	1 (0.3%)
Pyelonephritis Acute	1 (0.6%)	0	1 (0.3%)
Scrotal Abscess	1 (0.6%)	0	1 (0.3%)
Sinusitis	0	1 (0.6%)	1 (0.3%)
Injury, Poisoning And Procedural Complications	22 (12.9%)	15 (8.6%)	37 (10.8%)
Contusion	1 (0.6%)	2 (1.1%)	3 (0.9%)
Lower Limb Fracture	3 (1.8%)	0	3 (0.9%)

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Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
SOCs are sorted alphabetically and PTs by descending patient count in the total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.3: Summary of Medical History by SOC/PT
ITT2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Meniscus Injury	3 (1.8%)	0	3 (0.9%)
Pelvic Fracture	2 (1.2%)	1 (0.6%)	3 (0.9%)
Rib Fracture	1 (0.6%)	2 (1.1%)	3 (0.9%)
Eye Injury	1 (0.6%)	1 (0.6%)	2 (0.6%)
Femur Fracture	0	2 (1.1%)	2 (0.6%)
Spinal Fracture	1 (0.6%)	1 (0.6%)	2 (0.6%)
Tendon Rupture	2 (1.2%)	0	2 (0.6%)
Ankle Fracture	0	1 (0.6%)	1 (0.3%)
Asbestosis	1 (0.6%)	0	1 (0.3%)
Compression Fracture	1 (0.6%)	0	1 (0.3%)
Cystitis Radiation	1 (0.6%)	0	1 (0.3%)
Extradural Haematoma	1 (0.6%)	0	1 (0.3%)
Fall	0	1 (0.6%)	1 (0.3%)
Foreign Body In Eye	1 (0.6%)	0	1 (0.3%)
Fracture	1 (0.6%)	0	1 (0.3%)
Gun Shot Wound	1 (0.6%)	0	1 (0.3%)
Humerus Fracture	1 (0.6%)	0	1 (0.3%)
Injury	0	1 (0.6%)	1 (0.3%)
Joint Dislocation	1 (0.6%)	0	1 (0.3%)
Ligament Rupture	1 (0.6%)	0	1 (0.3%)
Lumbar Vertebral Fracture	0	1 (0.6%)	1 (0.3%)
Patella Fracture	0	1 (0.6%)	1 (0.3%)
Post Procedural Hypothyroidism	0	1 (0.6%)	1 (0.3%)
Procedural Pain	1 (0.6%)	0	1 (0.3%)
Skull Fractured Base	0	1 (0.6%)	1 (0.3%)
Stoma Site Pain	1 (0.6%)	0	1 (0.3%)
Stoma Site Pruritus	1 (0.6%)	0	1 (0.3%)
Tendon Injury	1 (0.6%)	0	1 (0.3%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
SOCs are sorted alphabetically and PTs by descending patient count in the total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.3: Summary of Medical History by SOC/PT
ITT2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Tooth Injury	1 (0.6%)	0	1 (0.3%)
Traumatic Lung Injury	1 (0.6%)	0	1 (0.3%)
Upper Limb Fracture	0	1 (0.6%)	1 (0.3%)
Urethral Stricture Traumatic	1 (0.6%)	0	1 (0.3%)
Wrist Fracture	0	1 (0.6%)	1 (0.3%)
Investigations	51 (30.0%)	50 (28.7%)	101 (29.4%)
Creatinine Renal Clearance Decreased	16 (9.4%)	27 (15.5%)	43 (12.5%)
Blood Creatinine Increased	9 (5.3%)	6 (3.4%)	15 (4.4%)
Blood Cholesterol Increased	7 (4.1%)	2 (1.1%)	9 (2.6%)
Weight Decreased	3 (1.8%)	3 (1.7%)	6 (1.7%)
Arthroscopy	3 (1.8%)	1 (0.6%)	4 (1.2%)
Amylase Increased	2 (1.2%)	0	2 (0.6%)
Angiocardiogram	1 (0.6%)	1 (0.6%)	2 (0.6%)
Blood Glucose Increased	1 (0.6%)	1 (0.6%)	2 (0.6%)
Colonoscopy	0	2 (1.1%)	2 (0.6%)
Computerised Tomogram Abnormal	1 (0.6%)	1 (0.6%)	2 (0.6%)
Computerised Tomogram Thorax Abnormal	0	2 (1.1%)	2 (0.6%)
Glomerular Filtration Rate Decreased	1 (0.6%)	1 (0.6%)	2 (0.6%)
Lymphocyte Count Decreased	1 (0.6%)	1 (0.6%)	2 (0.6%)
Prostatic Specific Antigen Increased	2 (1.2%)	0	2 (0.6%)
White Blood Cell Count Increased	1 (0.6%)	1 (0.6%)	2 (0.6%)
Aspartate Aminotransferase Increased	1 (0.6%)	0	1 (0.3%)
Biopsy Lymph Gland	1 (0.6%)	0	1 (0.3%)
Biopsy Prostate	0	1 (0.6%)	1 (0.3%)
Blood Albumin Increased	1 (0.6%)	0	1 (0.3%)
Blood Alkaline Phosphatase Increased	1 (0.6%)	0	1 (0.3%)
Blood Chloride Increased	1 (0.6%)	0	1 (0.3%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
SOCs are sorted alphabetically and PTs by descending patient count in the total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.3: Summary of Medical History by SOC/PT
ITT2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Blood Thyroid Stimulating Hormone Increased	1 (0.6%)	0	1 (0.3%)
Body Temperature Increased	1 (0.6%)	0	1 (0.3%)
Cardiac Murmur	1 (0.6%)	0	1 (0.3%)
Computerised Tomogram Liver Abnormal	0	1 (0.6%)	1 (0.3%)
Continuous Glucose Monitoring	1 (0.6%)	0	1 (0.3%)
Creatinine Renal Clearance	0	1 (0.6%)	1 (0.3%)
Cystoscopy	1 (0.6%)	0	1 (0.3%)
Ejection Fraction Decreased	1 (0.6%)	0	1 (0.3%)
Eosinophil Count Decreased	1 (0.6%)	0	1 (0.3%)
Faecal Occult Blood Positive	1 (0.6%)	0	1 (0.3%)
Fundoscopy	0	1 (0.6%)	1 (0.3%)
Glycosylated Haemoglobin Increased	0	1 (0.6%)	1 (0.3%)
Haematocrit Decreased	1 (0.6%)	0	1 (0.3%)
Haemoglobin Decreased	0	1 (0.6%)	1 (0.3%)
Heart Rate Irregular	1 (0.6%)	0	1 (0.3%)
Killip Classification	1 (0.6%)	0	1 (0.3%)
Monocyte Count Increased	1 (0.6%)	0	1 (0.3%)
Neutrophil Count Increased	1 (0.6%)	0	1 (0.3%)
Oesophagogastroscopy	0	1 (0.6%)	1 (0.3%)
Oxygen Consumption Increased	0	1 (0.6%)	1 (0.3%)
Platelet Count Increased	1 (0.6%)	0	1 (0.3%)
Protein Total Increased	1 (0.6%)	0	1 (0.3%)
Reticulocyte Count Decreased	1 (0.6%)	0	1 (0.3%)
Serum Ferritin Decreased	0	1 (0.6%)	1 (0.3%)
Smear Cervix Abnormal	1 (0.6%)	0	1 (0.3%)
Tri-Iodothyronine Decreased	1 (0.6%)	0	1 (0.3%)
Troponin I Increased	0	1 (0.6%)	1 (0.3%)
Ultrasound Prostate Abnormal	1 (0.6%)	0	1 (0.3%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
SOCs are sorted alphabetically and PTs by descending patient count in the total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.3: Summary of Medical History by SOC/PT
ITT2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Ureteroscopy	1 (0.6%)	0	1 (0.3%)
Vitamin B12 Decreased	0	1 (0.6%)	1 (0.3%)
Weight Increased	1 (0.6%)	0	1 (0.3%)
White Blood Cell Count Decreased	1 (0.6%)	0	1 (0.3%)
Metabolism And Nutrition Disorders	94 (55.3%)	84 (48.3%)	178 (51.7%)
Type 2 Diabetes Mellitus	29 (17.1%)	25 (14.4%)	54 (15.7%)
Dyslipidaemia	27 (15.9%)	20 (11.5%)	47 (13.7%)
Hyperlipidaemia	21 (12.4%)	21 (12.1%)	42 (12.2%)
Hypercholesterolaemia	12 (7.1%)	17 (9.8%)	29 (8.4%)
Diabetes Mellitus	15 (8.8%)	13 (7.5%)	28 (8.1%)
Obesity	8 (4.7%)	6 (3.4%)	14 (4.1%)
Gout	8 (4.7%)	2 (1.1%)	10 (2.9%)
Hyperuricaemia	4 (2.4%)	4 (2.3%)	8 (2.3%)
Decreased Appetite	4 (2.4%)	3 (1.7%)	7 (2.0%)
Hyperglycaemia	4 (2.4%)	1 (0.6%)	5 (1.5%)
Hypokalaemia	2 (1.2%)	2 (1.1%)	4 (1.2%)
Hyperkalaemia	2 (1.2%)	1 (0.6%)	3 (0.9%)
Vitamin D Deficiency	2 (1.2%)	1 (0.6%)	3 (0.9%)
Glucose Tolerance Impaired	1 (0.6%)	1 (0.6%)	2 (0.6%)
Impaired Fasting Glucose	1 (0.6%)	1 (0.6%)	2 (0.6%)
Lactose Intolerance	1 (0.6%)	1 (0.6%)	2 (0.6%)
Dehydration	1 (0.6%)	0	1 (0.3%)
Diabetic Metabolic Decompensation	0	1 (0.6%)	1 (0.3%)
Electrolyte Imbalance	0	1 (0.6%)	1 (0.3%)
Hypercalcaemia	0	1 (0.6%)	1 (0.3%)
Hypercreatininaemia	1 (0.6%)	0	1 (0.3%)
Hyponatraemia	1 (0.6%)	0	1 (0.3%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
SOCs are sorted alphabetically and PTs by descending patient count in the total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.3: Summary of Medical History by SOC/PT
ITT2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Insulin-Requiring Type 2 Diabetes Mellitus	1 (0.6%)	0	1 (0.3%)
Iron Overload	1 (0.6%)	0	1 (0.3%)
Overweight	0	1 (0.6%)	1 (0.3%)
Type 1 Diabetes Mellitus	1 (0.6%)	0	1 (0.3%)
Vitamin B12 Deficiency	1 (0.6%)	0	1 (0.3%)
Musculoskeletal And Connective Tissue Disorders	57 (33.5%)	42 (24.1%)	99 (28.8%)
Osteoarthritis	19 (11.2%)	4 (2.3%)	23 (6.7%)
Spinal Osteoarthritis	11 (6.5%)	10 (5.7%)	21 (6.1%)
Back Pain	13 (7.6%)	6 (3.4%)	19 (5.5%)
Arthralgia	6 (3.5%)	6 (3.4%)	12 (3.5%)
Arthritis	5 (2.9%)	5 (2.9%)	10 (2.9%)
Osteoporosis	2 (1.2%)	6 (3.4%)	8 (2.3%)
Intervertebral Disc Protrusion	4 (2.4%)	2 (1.1%)	6 (1.7%)
Intervertebral Disc Degeneration	5 (2.9%)	0	5 (1.5%)
Muscle Spasms	5 (2.9%)	0	5 (1.5%)
Osteochondrosis	3 (1.8%)	2 (1.1%)	5 (1.5%)
Pain In Extremity	3 (1.8%)	2 (1.1%)	5 (1.5%)
Dupuytren's Contracture	1 (0.6%)	1 (0.6%)	2 (0.6%)
Flank Pain	1 (0.6%)	1 (0.6%)	2 (0.6%)
Intervertebral Disc Disorder	1 (0.6%)	1 (0.6%)	2 (0.6%)
Osteopenia	1 (0.6%)	1 (0.6%)	2 (0.6%)
Rheumatoid Arthritis	1 (0.6%)	1 (0.6%)	2 (0.6%)
Rotator Cuff Syndrome	1 (0.6%)	1 (0.6%)	2 (0.6%)
Spondylolisthesis	2 (1.2%)	0	2 (0.6%)
Bone Cyst	1 (0.6%)	0	1 (0.3%)
Bursitis	1 (0.6%)	0	1 (0.3%)
Cervical Spinal Stenosis	0	1 (0.6%)	1 (0.3%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
SOCs are sorted alphabetically and PTs by descending patient count in the total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.3: Summary of Medical History by SOC/PT
ITT2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Exostosis	1 (0.6%)	0	1 (0.3%)
Gouty Arthritis	1 (0.6%)	0	1 (0.3%)
Kyphoscoliosis	0	1 (0.6%)	1 (0.3%)
Lumbar Spinal Stenosis	0	1 (0.6%)	1 (0.3%)
Musculoskeletal Chest Pain	0	1 (0.6%)	1 (0.3%)
Myalgia	1 (0.6%)	0	1 (0.3%)
Neck Pain	0	1 (0.6%)	1 (0.3%)
Periarthritis	0	1 (0.6%)	1 (0.3%)
Scoliosis	1 (0.6%)	0	1 (0.3%)
Spinal Deformity	0	1 (0.6%)	1 (0.3%)
Spinal Disorder	1 (0.6%)	0	1 (0.3%)
Spinal Pain	0	1 (0.6%)	1 (0.3%)
Spinal Stenosis	1 (0.6%)	0	1 (0.3%)
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)	31 (18.2%)	37 (21.3%)	68 (19.8%)
Prostate Cancer	10 (5.9%)	5 (2.9%)	15 (4.4%)
Adrenal Adenoma	4 (2.4%)	4 (2.3%)	8 (2.3%)
Colon Cancer	4 (2.4%)	2 (1.1%)	6 (1.7%)
Gastric Cancer	3 (1.8%)	2 (1.1%)	5 (1.5%)
Haemangioma Of Liver	1 (0.6%)	3 (1.7%)	4 (1.2%)
Lipoma	2 (1.2%)	2 (1.1%)	4 (1.2%)
Uterine Leiomyoma	1 (0.6%)	2 (1.1%)	3 (0.9%)
Basal Cell Carcinoma	1 (0.6%)	1 (0.6%)	2 (0.6%)
Breast Cancer	0	2 (1.1%)	2 (0.6%)
Lung Neoplasm Malignant	1 (0.6%)	1 (0.6%)	2 (0.6%)
Malignant Melanoma	1 (0.6%)	1 (0.6%)	2 (0.6%)
Prostatic Adenoma	0	2 (1.1%)	2 (0.6%)
Squamous Cell Carcinoma	1 (0.6%)	1 (0.6%)	2 (0.6%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
SOCs are sorted alphabetically and PTs by descending patient count in the total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.3: Summary of Medical History by SOC/PT
ITT2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Adenocarcinoma	0	1 (0.6%)	1 (0.3%)
Adenocarcinoma Of Colon	1 (0.6%)	0	1 (0.3%)
Adrenal Neoplasm	0	1 (0.6%)	1 (0.3%)
Benign Soft Tissue Neoplasm	0	1 (0.6%)	1 (0.3%)
Cancer Pain	0	1 (0.6%)	1 (0.3%)
Choroid Melanoma	1 (0.6%)	0	1 (0.3%)
Clear Cell Renal Cell Carcinoma	0	1 (0.6%)	1 (0.3%)
Colorectal Adenoma	0	1 (0.6%)	1 (0.3%)
Endometrial Cancer	0	1 (0.6%)	1 (0.3%)
Follicular Lymphoma	1 (0.6%)	0	1 (0.3%)
Gastrointestinal Tract Adenoma	0	1 (0.6%)	1 (0.3%)
Haemangioma Of Skin	0	1 (0.6%)	1 (0.3%)
Keratoacanthoma	0	1 (0.6%)	1 (0.3%)
Laryngeal Squamous Cell Carcinoma	1 (0.6%)	0	1 (0.3%)
Lung Adenocarcinoma	0	1 (0.6%)	1 (0.3%)
Lymphoma	1 (0.6%)	0	1 (0.3%)
Malignant Melanoma Stage 0	1 (0.6%)	0	1 (0.3%)
Nasal Sinus Cancer	0	1 (0.6%)	1 (0.3%)
Ovarian Cancer	1 (0.6%)	0	1 (0.3%)
Pleural Mesothelioma	1 (0.6%)	0	1 (0.3%)
Renal Perivascular Epithelioid Cell Tumour	0	1 (0.6%)	1 (0.3%)
Squamous Cell Carcinoma Of Skin	0	1 (0.6%)	1 (0.3%)
Tonsil Cancer	1 (0.6%)	0	1 (0.3%)
Transitional Cell Cancer Of The Renal Pelvis And Ureter	0	1 (0.6%)	1 (0.3%)
Transitional Cell Carcinoma	0	1 (0.6%)	1 (0.3%)
Tumour Obstruction	0	1 (0.6%)	1 (0.3%)
Tumour Pain	0	1 (0.6%)	1 (0.3%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
SOCs are sorted alphabetically and PTs by descending patient count in the total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.3: Summary of Medical History by SOC/PT
ITT2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Nervous System Disorders	39 (22.9%)	46 (26.4%)	85 (24.7%)
Cerebrovascular Accident	3 (1.8%)	5 (2.9%)	8 (2.3%)
Peripheral Sensory Neuropathy	4 (2.4%)	4 (2.3%)	8 (2.3%)
Carotid Artery Stenosis	5 (2.9%)	2 (1.1%)	7 (2.0%)
Migraine	5 (2.9%)	1 (0.6%)	6 (1.7%)
Cerebral Arteriosclerosis	3 (1.8%)	2 (1.1%)	5 (1.5%)
Parkinson's Disease	1 (0.6%)	4 (2.3%)	5 (1.5%)
Cerebral Infarction	1 (0.6%)	3 (1.7%)	4 (1.2%)
Cerebral Ischaemia	1 (0.6%)	3 (1.7%)	4 (1.2%)
Memory Impairment	2 (1.2%)	2 (1.1%)	4 (1.2%)
Carpal Tunnel Syndrome	2 (1.2%)	1 (0.6%)	3 (0.9%)
Cerebrovascular Disorder	1 (0.6%)	2 (1.1%)	3 (0.9%)
Cognitive Disorder	2 (1.2%)	1 (0.6%)	3 (0.9%)
Dizziness	2 (1.2%)	1 (0.6%)	3 (0.9%)
Encephalopathy	2 (1.2%)	1 (0.6%)	3 (0.9%)
Headache	2 (1.2%)	1 (0.6%)	3 (0.9%)
Neuropathy Peripheral	2 (1.2%)	1 (0.6%)	3 (0.9%)
Restless Legs Syndrome	1 (0.6%)	2 (1.1%)	3 (0.9%)
Diabetic Neuropathy	2 (1.2%)	0	2 (0.6%)
Dysgeusia	2 (1.2%)	0	2 (0.6%)
Hypoaesthesia	0	2 (1.1%)	2 (0.6%)
Ischaemic Stroke	0	2 (1.1%)	2 (0.6%)
Myelopathy	0	2 (1.1%)	2 (0.6%)
Paraesthesia	2 (1.2%)	0	2 (0.6%)
Polyneuropathy	0	2 (1.1%)	2 (0.6%)
Radiculopathy	0	2 (1.1%)	2 (0.6%)
Transient Ischaemic Attack	2 (1.2%)	0	2 (0.6%)
Vascular Encephalopathy	1 (0.6%)	1 (0.6%)	2 (0.6%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
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SOCs are sorted alphabetically and PTs by descending patient count in the total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.3: Summary of Medical History by SOC/PT
ITT2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Amnesia	0	1 (0.6%)	1 (0.3%)
Balance Disorder	0	1 (0.6%)	1 (0.3%)
Basal Ganglia Infarction	1 (0.6%)	0	1 (0.3%)
Cluster Headache	0	1 (0.6%)	1 (0.3%)
Dementia	0	1 (0.6%)	1 (0.3%)
Disturbance In Attention	0	1 (0.6%)	1 (0.3%)
Dizziness Postural	0	1 (0.6%)	1 (0.3%)
Epilepsy	1 (0.6%)	0	1 (0.3%)
Essential Tremor	1 (0.6%)	0	1 (0.3%)
Facial Paralysis	0	1 (0.6%)	1 (0.3%)
Hemiplegia	0	1 (0.6%)	1 (0.3%)
Intracranial Aneurysm	1 (0.6%)	0	1 (0.3%)
Lacunar Infarction	1 (0.6%)	0	1 (0.3%)
Lacunar Stroke	1 (0.6%)	0	1 (0.3%)
Lumbar Radiculopathy	0	1 (0.6%)	1 (0.3%)
Motor Dysfunction	1 (0.6%)	0	1 (0.3%)
Nerve Compression	0	1 (0.6%)	1 (0.3%)
Neuralgia	1 (0.6%)	0	1 (0.3%)
Sciatic Nerve Neuropathy	1 (0.6%)	0	1 (0.3%)
Seizure	0	1 (0.6%)	1 (0.3%)
Spinal Claudication	1 (0.6%)	0	1 (0.3%)
Spinal Cord Compression	0	1 (0.6%)	1 (0.3%)
Syncope	0	1 (0.6%)	1 (0.3%)
Thecal Sac Compression	0	1 (0.6%)	1 (0.3%)
Vertebrobasilar Insufficiency	0	1 (0.6%)	1 (0.3%)
Psychiatric Disorders	25 (14.7%)	35 (20.1%)	60 (17.4%)
Depression	8 (4.7%)	14 (8.0%)	22 (6.4%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
SOCs are sorted alphabetically and PTs by descending patient count in the total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.3: Summary of Medical History by SOC/PT
ITT2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Insomnia	11 (6.5%)	7 (4.0%)	18 (5.2%)
Anxiety	8 (4.7%)	9 (5.2%)	17 (4.9%)
Sleep Disorder	2 (1.2%)	3 (1.7%)	5 (1.5%)
Anxiety Disorder	0	2 (1.1%)	2 (0.6%)
Attention Deficit Hyperactivity Disorder	1 (0.6%)	1 (0.6%)	2 (0.6%)
Panic Disorder	0	2 (1.1%)	2 (0.6%)
Tobacco Abuse	2 (1.2%)	0	2 (0.6%)
Adjustment Disorder With Depressed Mood	0	1 (0.6%)	1 (0.3%)
Alcohol Abuse	0	1 (0.6%)	1 (0.3%)
Alcoholism	0	1 (0.6%)	1 (0.3%)
Confusional State	0	1 (0.6%)	1 (0.3%)
Dyssomnia	0	1 (0.6%)	1 (0.3%)
Generalised Anxiety Disorder	0	1 (0.6%)	1 (0.3%)
Mood Swings	0	1 (0.6%)	1 (0.3%)
Obsessive-Compulsive Disorder	1 (0.6%)	0	1 (0.3%)
Schizophrenia	0	1 (0.6%)	1 (0.3%)
Renal And Urinary Disorders	106 (62.4%)	101 (58.0%)	207 (60.2%)
Chronic Kidney Disease	31 (18.2%)	29 (16.7%)	60 (17.4%)
Hydronephrosis	24 (14.1%)	24 (13.8%)	48 (14.0%)
Haematuria	24 (14.1%)	23 (13.2%)	47 (13.7%)
Renal Impairment	29 (17.1%)	16 (9.2%)	45 (13.1%)
Renal Cyst	14 (8.2%)	15 (8.6%)	29 (8.4%)
Pollakiuria	15 (8.8%)	12 (6.9%)	27 (7.8%)
Dysuria	7 (4.1%)	12 (6.9%)	19 (5.5%)
Micturition Urgency	11 (6.5%)	6 (3.4%)	17 (4.9%)
Renal Failure	6 (3.5%)	4 (2.3%)	10 (2.9%)
Urinary Incontinence	7 (4.1%)	3 (1.7%)	10 (2.9%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
SOCs are sorted alphabetically and PTs by descending patient count in the total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.3: Summary of Medical History by SOC/PT
ITT2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Hypertonic Bladder	5 (2.9%)	3 (1.7%)	8 (2.3%)
Nephrolithiasis	3 (1.8%)	5 (2.9%)	8 (2.3%)
Nocturia	4 (2.4%)	4 (2.3%)	8 (2.3%)
Calculus Urinary	0	4 (2.3%)	4 (1.2%)
Cystitis Noninfective	3 (1.8%)	1 (0.6%)	4 (1.2%)
Urethral Stenosis	2 (1.2%)	2 (1.1%)	4 (1.2%)
Urinary Retention	3 (1.8%)	1 (0.6%)	4 (1.2%)
Acute Kidney Injury	1 (0.6%)	2 (1.1%)	3 (0.9%)
Bladder Hypertrophy	1 (0.6%)	2 (1.1%)	3 (0.9%)
Renal Atrophy	0	3 (1.7%)	3 (0.9%)
Single Functional Kidney	1 (0.6%)	2 (1.1%)	3 (0.9%)
Urinary Tract Pain	1 (0.6%)	2 (1.1%)	3 (0.9%)
Bladder Diverticulum	1 (0.6%)	1 (0.6%)	2 (0.6%)
Bladder Spasm	2 (1.2%)	0	2 (0.6%)
Proteinuria	1 (0.6%)	1 (0.6%)	2 (0.6%)
Urethral Pain	1 (0.6%)	1 (0.6%)	2 (0.6%)
Urinary Tract Obstruction	2 (1.2%)	0	2 (0.6%)
Azotaemia	1 (0.6%)	0	1 (0.3%)
Bladder Hyperaemia	1 (0.6%)	0	1 (0.3%)
Bladder Irritation	1 (0.6%)	0	1 (0.3%)
Bladder Mass	1 (0.6%)	0	1 (0.3%)
Bladder Pain	1 (0.6%)	0	1 (0.3%)
Bladder Perforation	1 (0.6%)	0	1 (0.3%)
Calculus Bladder	1 (0.6%)	0	1 (0.3%)
Cystitis Interstitial	1 (0.6%)	0	1 (0.3%)
Incontinence	0	1 (0.6%)	1 (0.3%)
Lower Urinary Tract Symptoms	1 (0.6%)	0	1 (0.3%)
Microalbuminuria	0	1 (0.6%)	1 (0.3%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
SOCs are sorted alphabetically and PTs by descending patient count in the total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.3: Summary of Medical History by SOC/PT
ITT2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Nephrosclerosis	0	1 (0.6%)	1 (0.3%)
Oliguria	0	1 (0.6%)	1 (0.3%)
Polyuria	0	1 (0.6%)	1 (0.3%)
Postrenal Failure	1 (0.6%)	0	1 (0.3%)
Pyelocaliectasis	0	1 (0.6%)	1 (0.3%)
Renal Colic	1 (0.6%)	0	1 (0.3%)
Ureteric Dilatation	0	1 (0.6%)	1 (0.3%)
Ureteric Obstruction	1 (0.6%)	0	1 (0.3%)
Ureterolithiasis	0	1 (0.6%)	1 (0.3%)
Urine Flow Decreased	1 (0.6%)	0	1 (0.3%)
Reproductive System And Breast Disorders	44 (25.9%)	42 (24.1%)	86 (25.0%)
Benign Prostatic Hyperplasia	36 (21.2%)	36 (20.7%)	72 (20.9%)
Pelvic Pain	5 (2.9%)	2 (1.1%)	7 (2.0%)
Prostatitis	2 (1.2%)	2 (1.1%)	4 (1.2%)
Erectile Dysfunction	1 (0.6%)	1 (0.6%)	2 (0.6%)
Prostatomegaly	0	2 (1.1%)	2 (0.6%)
Abnormal Uterine Bleeding	1 (0.6%)	0	1 (0.3%)
Calculus Prostatic	1 (0.6%)	0	1 (0.3%)
Epididymal Cyst	0	1 (0.6%)	1 (0.3%)
Genital Burning Sensation	1 (0.6%)	0	1 (0.3%)
Gynaecomastia	0	1 (0.6%)	1 (0.3%)
Heavy Menstrual Bleeding	0	1 (0.6%)	1 (0.3%)
Ovarian Cyst	0	1 (0.6%)	1 (0.3%)
Prostatic Disorder	1 (0.6%)	0	1 (0.3%)
Sexual Dysfunction	1 (0.6%)	0	1 (0.3%)
Testicular Hypertrophy	1 (0.6%)	0	1 (0.3%)
Testicular Torsion	1 (0.6%)	0	1 (0.3%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
SOCs are sorted alphabetically and PTs by descending patient count in the total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.3: Summary of Medical History by SOC/PT
ITT2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Varicocele	1 (0.6%)	0	1 (0.3%)
Vulvovaginal Dryness	1 (0.6%)	0	1 (0.3%)
Vulvovaginal Pain	0	1 (0.6%)	1 (0.3%)
Respiratory, Thoracic And Mediastinal Disorders	49 (28.8%)	54 (31.0%)	103 (29.9%)
Chronic Obstructive Pulmonary Disease	15 (8.8%)	19 (10.9%)	34 (9.9%)
Asthma	3 (1.8%)	10 (5.7%)	13 (3.8%)
Emphysema	3 (1.8%)	7 (4.0%)	10 (2.9%)
Sleep Apnoea Syndrome	3 (1.8%)	5 (2.9%)	8 (2.3%)
Bronchitis Chronic	4 (2.4%)	2 (1.1%)	6 (1.7%)
Dyspnoea	5 (2.9%)	1 (0.6%)	6 (1.7%)
Pulmonary Embolism	4 (2.4%)	2 (1.1%)	6 (1.7%)
Pulmonary Mass	3 (1.8%)	3 (1.7%)	6 (1.7%)
Cough	3 (1.8%)	2 (1.1%)	5 (1.5%)
Obstructive Sleep Apnoea Syndrome	5 (2.9%)	0	5 (1.5%)
Rhinitis Allergic	3 (1.8%)	1 (0.6%)	4 (1.2%)
Atelectasis	1 (0.6%)	2 (1.1%)	3 (0.9%)
Pulmonary Fibrosis	0	3 (1.7%)	3 (0.9%)
Pulmonary Granuloma	1 (0.6%)	2 (1.1%)	3 (0.9%)
Bronchiectasis	0	2 (1.1%)	2 (0.6%)
Dyspnoea Exertional	1 (0.6%)	1 (0.6%)	2 (0.6%)
Lung Disorder	1 (0.6%)	1 (0.6%)	2 (0.6%)
Pleural Effusion	0	2 (1.1%)	2 (0.6%)
Pulmonary Hypertension	1 (0.6%)	1 (0.6%)	2 (0.6%)
Acquired Diaphragmatic Eventration	0	1 (0.6%)	1 (0.3%)
Dysphonia	0	1 (0.6%)	1 (0.3%)
Epiglottic Cyst	1 (0.6%)	0	1 (0.3%)
Oropharyngeal Fistula	1 (0.6%)	0	1 (0.3%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
SOCs are sorted alphabetically and PTs by descending patient count in the total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.3: Summary of Medical History by SOC/PT
ITT2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Oropharyngeal Pain	1 (0.6%)	0	1 (0.3%)
Pharyngeal Hypertrophy	1 (0.6%)	0	1 (0.3%)
Productive Cough	0	1 (0.6%)	1 (0.3%)
Vocal Cord Atrophy	0	1 (0.6%)	1 (0.3%)
Skin And Subcutaneous Tissue Disorders	15 (8.8%)	10 (5.7%)	25 (7.3%)
Psoriasis	5 (2.9%)	2 (1.1%)	7 (2.0%)
Dry Skin	2 (1.2%)	1 (0.6%)	3 (0.9%)
Rash	2 (1.2%)	1 (0.6%)	3 (0.9%)
Brow Ptosis	1 (0.6%)	1 (0.6%)	2 (0.6%)
Dermatitis	1 (0.6%)	1 (0.6%)	2 (0.6%)
Pruritus	1 (0.6%)	1 (0.6%)	2 (0.6%)
Actinic Keratosis	1 (0.6%)	0	1 (0.3%)
Dermatitis Contact	1 (0.6%)	0	1 (0.3%)
Eczema	1 (0.6%)	0	1 (0.3%)
Rash Maculo-Papular	0	1 (0.6%)	1 (0.3%)
Skin Exfoliation	1 (0.6%)	0	1 (0.3%)
Skin Hyperpigmentation	0	1 (0.6%)	1 (0.3%)
Skin Lesion	1 (0.6%)	0	1 (0.3%)
Skin Ulcer	0	1 (0.6%)	1 (0.3%)
Xeroderma	0	1 (0.6%)	1 (0.3%)
Social Circumstances	3 (1.8%)	2 (1.1%)	5 (1.5%)
Menopause	1 (0.6%)	1 (0.6%)	2 (0.6%)
Hearing Aid User	1 (0.6%)	0	1 (0.3%)
Postmenopause	1 (0.6%)	0	1 (0.3%)
Tobacco User	0	1 (0.6%)	1 (0.3%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
SOCs are sorted alphabetically and PTs by descending patient count in the total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.3: Summary of Medical History by SOC/PT
ITT2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Surgical And Medical Procedures	65 (38.2%)	71 (40.8%)	136 (39.5%)
Nephrostomy	11 (6.5%)	11 (6.3%)	22 (6.4%)
Cataract Operation	8 (4.7%)	6 (3.4%)	14 (4.1%)
Inguinal Hernia Repair	6 (3.5%)	6 (3.4%)	12 (3.5%)
Appendicectomy	3 (1.8%)	6 (3.4%)	9 (2.6%)
Coronary Arterial Stent Insertion	2 (1.2%)	7 (4.0%)	9 (2.6%)
Knee Arthroplasty	4 (2.4%)	5 (2.9%)	9 (2.6%)
Transurethral Prostatectomy	4 (2.4%)	5 (2.9%)	9 (2.6%)
Coronary Artery Bypass	3 (1.8%)	5 (2.9%)	8 (2.3%)
Cholecystectomy	2 (1.2%)	5 (2.9%)	7 (2.0%)
Hernia Repair	3 (1.8%)	4 (2.3%)	7 (2.0%)
Skin Neoplasm Excision	4 (2.4%)	1 (0.6%)	5 (1.5%)
Tonsillectomy	2 (1.2%)	3 (1.7%)	5 (1.5%)
Cardiac Pacemaker Insertion	3 (1.8%)	1 (0.6%)	4 (1.2%)
Hip Arthroplasty	4 (2.4%)	0	4 (1.2%)
Hysterectomy	0	4 (2.3%)	4 (1.2%)
Thyroidectomy	2 (1.2%)	2 (1.1%)	4 (1.2%)
Ureteral Stent Insertion	2 (1.2%)	2 (1.1%)	4 (1.2%)
Aortic Valve Replacement	1 (0.6%)	2 (1.1%)	3 (0.9%)
Cancer Surgery	2 (1.2%)	1 (0.6%)	3 (0.9%)
Carotid Artery Stent Insertion	2 (1.2%)	1 (0.6%)	3 (0.9%)
Coronary Angioplasty	2 (1.2%)	1 (0.6%)	3 (0.9%)
Internal Fixation Of Fracture	3 (1.8%)	0	3 (0.9%)
Large Intestinal Polypectomy	1 (0.6%)	2 (1.1%)	3 (0.9%)
Nasal Septal Operation	1 (0.6%)	2 (1.1%)	3 (0.9%)
Radical Prostatectomy	2 (1.2%)	1 (0.6%)	3 (0.9%)
Stent Placement	3 (1.8%)	0	3 (0.9%)
Aortic Aneurysm Repair	1 (0.6%)	1 (0.6%)	2 (0.6%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
SOCs are sorted alphabetically and PTs by descending patient count in the total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.3: Summary of Medical History by SOC/PT
ITT2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Arterial Stent Insertion	0	2 (1.1%)	2 (0.6%)
Carotid Endarterectomy	1 (0.6%)	1 (0.6%)	2 (0.6%)
Dental Implantation	1 (0.6%)	1 (0.6%)	2 (0.6%)
Eye Operation	2 (1.2%)	0	2 (0.6%)
Fracture Treatment	1 (0.6%)	1 (0.6%)	2 (0.6%)
Gastrectomy	1 (0.6%)	1 (0.6%)	2 (0.6%)
Haemorrhoid Operation	1 (0.6%)	1 (0.6%)	2 (0.6%)
Hydrocele Operation	1 (0.6%)	1 (0.6%)	2 (0.6%)
Intraocular Lens Implant	0	2 (1.1%)	2 (0.6%)
Prostatectomy	2 (1.2%)	0	2 (0.6%)
Pulmonary Resection	0	2 (1.1%)	2 (0.6%)
Tenoplasty	2 (1.2%)	0	2 (0.6%)
Umbilical Hernia Repair	1 (0.6%)	1 (0.6%)	2 (0.6%)
Urethrotomy	1 (0.6%)	1 (0.6%)	2 (0.6%)
Vasectomy	2 (1.2%)	0	2 (0.6%)
Abscess Drainage	0	1 (0.6%)	1 (0.3%)
Adenoidectomy	1 (0.6%)	0	1 (0.3%)
Anal Polypectomy	0	1 (0.6%)	1 (0.3%)
Ankle Operation	0	1 (0.6%)	1 (0.3%)
Aortic Bypass	1 (0.6%)	0	1 (0.3%)
Aortic Valve Repair	1 (0.6%)	0	1 (0.3%)
Benign Tumour Excision	0	1 (0.6%)	1 (0.3%)
Bladder Lesion Excision	0	1 (0.6%)	1 (0.3%)
Bone Lesion Excision	1 (0.6%)	0	1 (0.3%)
Bone Operation	0	1 (0.6%)	1 (0.3%)
Brachytherapy	1 (0.6%)	0	1 (0.3%)
Bunion Operation	0	1 (0.6%)	1 (0.3%)
Caesarean Section	0	1 (0.6%)	1 (0.3%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
SOCs are sorted alphabetically and PTs by descending patient count in the total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.3: Summary of Medical History by SOC/PT
ITT2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Cardiac Ablation	1 (0.6%)	0	1 (0.3%)
Carotid Angioplasty	0	1 (0.6%)	1 (0.3%)
Carpal Tunnel Decompression	1 (0.6%)	0	1 (0.3%)
Colon Operation	0	1 (0.6%)	1 (0.3%)
Craniotomy	1 (0.6%)	0	1 (0.3%)
Cyst Removal	1 (0.6%)	0	1 (0.3%)
Cystostomy	0	1 (0.6%)	1 (0.3%)
Duodenal Ulcer Repair	1 (0.6%)	0	1 (0.3%)
Ear Operation	0	1 (0.6%)	1 (0.3%)
Eye Excision	0	1 (0.6%)	1 (0.3%)
Haemostasis	0	1 (0.6%)	1 (0.3%)
Hysterosalpingo-Oophorectomy	0	1 (0.6%)	1 (0.3%)
Implantable Defibrillator Insertion	0	1 (0.6%)	1 (0.3%)
Intervertebral Disc Operation	0	1 (0.6%)	1 (0.3%)
Keratomileusis	1 (0.6%)	0	1 (0.3%)
Knee Operation	0	1 (0.6%)	1 (0.3%)
Laparotomy	1 (0.6%)	0	1 (0.3%)
Laryngeal Operation	1 (0.6%)	0	1 (0.3%)
Ligament Operation	1 (0.6%)	0	1 (0.3%)
Lithotripsy	0	1 (0.6%)	1 (0.3%)
Lymphadenectomy	0	1 (0.6%)	1 (0.3%)
Mastectomy	0	1 (0.6%)	1 (0.3%)
Medical Device Removal	1 (0.6%)	0	1 (0.3%)
Meniscus Operation	1 (0.6%)	0	1 (0.3%)
Meniscus Removal	1 (0.6%)	0	1 (0.3%)
Microfracture Surgery	1 (0.6%)	0	1 (0.3%)
Micrographic Skin Surgery	0	1 (0.6%)	1 (0.3%)
Neck Surgery	0	1 (0.6%)	1 (0.3%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
SOCs are sorted alphabetically and PTs by descending patient count in the total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.3: Summary of Medical History by SOC/PT
ITT2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Nephrectomy	0	1 (0.6%)	1 (0.3%)
Nephroureterectomy	0	1 (0.6%)	1 (0.3%)
Oophorectomy	0	1 (0.6%)	1 (0.3%)
Percutaneous Coronary Intervention	0	1 (0.6%)	1 (0.3%)
Peripheral Artery Stent Insertion	1 (0.6%)	0	1 (0.3%)
Polypectomy	1 (0.6%)	0	1 (0.3%)
Prosthetic Vessel Implantation	0	1 (0.6%)	1 (0.3%)
Radiochemotherapy	1 (0.6%)	0	1 (0.3%)
Radiotherapy To Thyroid	0	1 (0.6%)	1 (0.3%)
Rectal Polypectomy	0	1 (0.6%)	1 (0.3%)
Renal Stone Removal	0	1 (0.6%)	1 (0.3%)
Retinal Laser Coagulation	0	1 (0.6%)	1 (0.3%)
Spinal Laminectomy	0	1 (0.6%)	1 (0.3%)
Splenectomy	0	1 (0.6%)	1 (0.3%)
Tenotomy	1 (0.6%)	0	1 (0.3%)
Therapeutic Embolisation	0	1 (0.6%)	1 (0.3%)
Thoracic Cavity Drainage	0	1 (0.6%)	1 (0.3%)
Thrombectomy	1 (0.6%)	0	1 (0.3%)
Tooth Extraction	1 (0.6%)	0	1 (0.3%)
Transmyocardial Revascularisation	0	1 (0.6%)	1 (0.3%)
Transurethral Bladder Resection	0	1 (0.6%)	1 (0.3%)
Tumour Excision	1 (0.6%)	0	1 (0.3%)
Turbinoplasty	1 (0.6%)	0	1 (0.3%)
Urethrectomy	0	1 (0.6%)	1 (0.3%)
Vocal Cordectomy	1 (0.6%)	0	1 (0.3%)
Wisdom Teeth Removal	0	1 (0.6%)	1 (0.3%)
Vascular Disorders	116 (68.2%)	121 (69.5%)	237 (68.9%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
SOCs are sorted alphabetically and PTs by descending patient count in the total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.3: Summary of Medical History by SOC/PT
ITT2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Hypertension	108 (63.5%)	114 (65.5%)	222 (64.5%)
Aortic Aneurysm	3 (1.8%)	9 (5.2%)	12 (3.5%)
Arteriosclerosis	5 (2.9%)	7 (4.0%)	12 (3.5%)
Aortic Arteriosclerosis	3 (1.8%)	6 (3.4%)	9 (2.6%)
Varicose Vein	3 (1.8%)	3 (1.7%)	6 (1.7%)
Peripheral Artery Aneurysm	2 (1.2%)	2 (1.1%)	4 (1.2%)
Intermittent Claudication	2 (1.2%)	1 (0.6%)	3 (0.9%)
Peripheral Arterial Occlusive Disease	1 (0.6%)	2 (1.1%)	3 (0.9%)
Peripheral Venous Disease	3 (1.8%)	0	3 (0.9%)
Deep Vein Thrombosis	2 (1.2%)	0	2 (0.6%)
Essential Hypertension	1 (0.6%)	1 (0.6%)	2 (0.6%)
Hypertensive Angiopathy	1 (0.6%)	1 (0.6%)	2 (0.6%)
Iliac Artery Occlusion	1 (0.6%)	1 (0.6%)	2 (0.6%)
Peripheral Vascular Disorder	1 (0.6%)	1 (0.6%)	2 (0.6%)
Angiosclerosis	0	1 (0.6%)	1 (0.3%)
Aortic Dilatation	0	1 (0.6%)	1 (0.3%)
Aortic Stenosis	0	1 (0.6%)	1 (0.3%)
Aortic Thrombosis	0	1 (0.6%)	1 (0.3%)
Aortic Wall Hypertrophy	0	1 (0.6%)	1 (0.3%)
Brachiocephalic Arteriosclerosis	1 (0.6%)	0	1 (0.3%)
Embolism	1 (0.6%)	0	1 (0.3%)
Hot Flush	1 (0.6%)	0	1 (0.3%)
Iliac Artery Arteriosclerosis	0	1 (0.6%)	1 (0.3%)
Infarction	1 (0.6%)	0	1 (0.3%)
Peripheral Artery Thrombosis	0	1 (0.6%)	1 (0.3%)
Superficial Vein Thrombosis	0	1 (0.6%)	1 (0.3%)
Thrombosis	1 (0.6%)	0	1 (0.3%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
SOCs are sorted alphabetically and PTs by descending patient count in the total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.4: Summary of Previous Therapies
ITT2 Analysis Set

Therapeutic Subgroup	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Overall	154 (90.6%)	143 (82.2%)	297 (86.3%)
Agents Acting On The Renin-Angiotensin System	76 (44.7%)	78 (44.8%)	154 (44.8%)
All Other Non-Therapeutic Products	13 (7.6%)	7 (4.0%)	20 (5.8%)
All Other Therapeutic Products	15 (8.8%)	16 (9.2%)	31 (9.0%)
Analgesics	77 (45.3%)	74 (42.5%)	151 (43.9%)
Anesthetics	1 (0.6%)	2 (1.1%)	3 (0.9%)
Anti-Acne Preparations	4 (2.4%)	8 (4.6%)	12 (3.5%)
Anti-Parkinson Drugs	2 (1.2%)	5 (2.9%)	7 (2.0%)
Antianemic Preparations	21 (12.4%)	17 (9.8%)	38 (11.0%)
Antibacterials For Systemic Use	11 (6.5%)	28 (16.1%)	39 (11.3%)
Antibiotics And Chemotherapeutics For Dermatological Use	5 (2.9%)	11 (6.3%)	16 (4.7%)
Antidiarrheals, Intestinal Antiinflammatory/Antiinfective Agents	10 (5.9%)	6 (3.4%)	16 (4.7%)
Antiemetics And Antinauseants	25 (14.7%)	10 (5.7%)	35 (10.2%)
Antiepileptics	16 (9.4%)	13 (7.5%)	29 (8.4%)
Antifungals For Dermatological Use	3 (1.8%)	2 (1.1%)	5 (1.5%)
Antigout Preparations	12 (7.1%)	12 (6.9%)	24 (7.0%)
Antihemorrhagics	3 (1.8%)	6 (3.4%)	9 (2.6%)
Antihistamines For Systemic Use	10 (5.9%)	10 (5.7%)	20 (5.8%)
Antihypertensives	13 (7.6%)	3 (1.7%)	16 (4.7%)
Antiinflammatory And Antirheumatic Products	17 (10.0%)	17 (9.8%)	34 (9.9%)
Antimycotics For Systemic Use	0	1 (0.6%)	1 (0.3%)
Antineoplastic Agents	4 (2.4%)	4 (2.3%)	8 (2.3%)
Antiobesity Preparations, Excl. Diet Products	4 (2.4%)	2 (1.1%)	6 (1.7%)
Antiprotozoals	3 (1.8%)	3 (1.7%)	6 (1.7%)
Antipruritics, Incl. Antihistamines, Anesthetics, Etc.	10 (5.9%)	9 (5.2%)	19 (5.5%)
Antipsoriatics	1 (0.6%)	2 (1.1%)	3 (0.9%)
Antiseptics And Disinfectants	1 (0.6%)	1 (0.6%)	2 (0.6%)

Abbreviations: ATC=anatomical therapeutic chemical; EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
Therapeutic subgroups (ATC 2nd level) are sorted alphabetically.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.4: Summary of Previous Therapies
ITT2 Analysis Set

Therapeutic Subgroup	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Antithrombotic Agents	57 (33.5%)	56 (32.2%)	113 (32.8%)
Antivirals For Systemic Use	1 (0.6%)	2 (1.1%)	3 (0.9%)
Appetite Stimulants	2 (1.2%)	0	2 (0.6%)
Beta Blocking Agents	48 (28.2%)	55 (31.6%)	103 (29.9%)
Bile And Liver Therapy	6 (3.5%)	7 (4.0%)	13 (3.8%)
Blood Substitutes And Perfusion Solutions	25 (14.7%)	22 (12.6%)	47 (13.7%)
Calcium Channel Blockers	37 (21.8%)	37 (21.3%)	74 (21.5%)
Calcium Homeostasis	2 (1.2%)	2 (1.1%)	4 (1.2%)
Cardiac Therapy	25 (14.7%)	28 (16.1%)	53 (15.4%)
Corticosteroids For Systemic Use	8 (4.7%)	3 (1.7%)	11 (3.2%)
Corticosteroids, Dermatological Preparations	14 (8.2%)	7 (4.0%)	21 (6.1%)
Cough And Cold Preparations	13 (7.6%)	10 (5.7%)	23 (6.7%)
Diagnostic Agents	3 (1.8%)	4 (2.3%)	7 (2.0%)
Diagnostic Radiopharmaceuticals	0	1 (0.6%)	1 (0.3%)
Digestives, Incl. Enzymes	3 (1.8%)	5 (2.9%)	8 (2.3%)
Diuretics	29 (17.1%)	28 (16.1%)	57 (16.6%)
Drugs For Acid Related Disorders	39 (22.9%)	47 (27.0%)	86 (25.0%)
Drugs For Constipation	25 (14.7%)	24 (13.8%)	49 (14.2%)
Drugs For Functional Gastrointestinal Disorders	9 (5.3%)	12 (6.9%)	21 (6.1%)
Drugs For Obstructive Airway Diseases	27 (15.9%)	25 (14.4%)	52 (15.1%)
Drugs For Treatment Of Bone Diseases	2 (1.2%)	2 (1.1%)	4 (1.2%)
Drugs Used In Diabetes	44 (25.9%)	32 (18.4%)	76 (22.1%)
Ectoparasiticides, Incl. Scabicides, Insecticides And Repellents	0	1 (0.6%)	1 (0.3%)
Emollients And Protectives	6 (3.5%)	4 (2.3%)	10 (2.9%)
Endocrine Therapy	3 (1.8%)	0	3 (0.9%)
General Nutrients	1 (0.6%)	3 (1.7%)	4 (1.2%)
Gynecological Antiinfectives And Antiseptics	8 (4.7%)	18 (10.3%)	26 (7.6%)
Homeopathic Preparation	22 (12.9%)	17 (9.8%)	39 (11.3%)

Abbreviations: ATC=anatomical therapeutic chemical; EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
Therapeutic subgroups (ATC 2nd level) are sorted alphabetically.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.4: Summary of Previous Therapies
ITT2 Analysis Set

Therapeutic Subgroup	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Immunostimulants	1 (0.6%)	0	1 (0.3%)
Immunosuppressants	2 (1.2%)	0	2 (0.6%)
Lipid Modifying Agents	68 (40.0%)	79 (45.4%)	147 (42.7%)
Medicated Dressings	11 (6.5%)	6 (3.4%)	17 (4.9%)
Mineral Supplements	22 (12.9%)	26 (14.9%)	48 (14.0%)
Muscle Relaxants	2 (1.2%)	6 (3.4%)	8 (2.3%)
Nasal Preparations	24 (14.1%)	18 (10.3%)	42 (12.2%)
Ophthalmological And Otological Preparations	8 (4.7%)	9 (5.2%)	17 (4.9%)
Ophthalmologicals	49 (28.8%)	56 (32.2%)	105 (30.5%)
Other Alimentary Tract And Metabolism Products	7 (4.1%)	11 (6.3%)	18 (5.2%)
Other Dermatological Preparations	28 (16.5%)	39 (22.4%)	67 (19.5%)
Other Drugs For Disorders Of The Musculo-Skeletal System	3 (1.8%)	0	3 (0.9%)
Other Gynecologicals	15 (8.8%)	18 (10.3%)	33 (9.6%)
Other Hematological Agents	1 (0.6%)	0	1 (0.3%)
Other Nervous System Drugs	25 (14.7%)	19 (10.9%)	44 (12.8%)
Other Respiratory System Products	1 (0.6%)	3 (1.7%)	4 (1.2%)
Otologicals	25 (14.7%)	15 (8.6%)	40 (11.6%)
Peripheral Vasodilators	2 (1.2%)	1 (0.6%)	3 (0.9%)
Preparations For Treatment Of Wounds And Ulcers	12 (7.1%)	8 (4.6%)	20 (5.8%)
Psychoanaleptics	19 (11.2%)	25 (14.4%)	44 (12.8%)
Psycholeptics	32 (18.8%)	34 (19.5%)	66 (19.2%)
Sex Hormones And Modulators Of The Genital System	3 (1.8%)	1 (0.6%)	4 (1.2%)
Stomatological Preparations	58 (34.1%)	52 (29.9%)	110 (32.0%)
Throat Preparations	5 (2.9%)	14 (8.0%)	19 (5.5%)
Thyroid Therapy	17 (10.0%)	18 (10.3%)	35 (10.2%)
Tonics	1 (0.6%)	2 (1.1%)	3 (0.9%)
Topical Products For Joint And Muscular Pain	53 (31.2%)	51 (29.3%)	104 (30.2%)
Unspecified Herbal And Traditional Medicine	9 (5.3%)	10 (5.7%)	19 (5.5%)

Abbreviations: ATC=anatomical therapeutic chemical; EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
Therapeutic subgroups (ATC 2nd level) are sorted alphabetically.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.4: Summary of Previous Therapies
ITT2 Analysis Set

Therapeutic Subgroup	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Urologicals	65 (38.2%)	54 (31.0%)	119 (34.6%)
Vaccines	4 (2.4%)	3 (1.7%)	7 (2.0%)
Vasoprotectives	21 (12.4%)	10 (5.7%)	31 (9.0%)
Vitamins	25 (14.7%)	23 (13.2%)	48 (14.0%)

Abbreviations: ATC=anatomical therapeutic chemical; EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
Therapeutic subgroups (ATC 2nd level) are sorted alphabetically.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.5: Summary of Concomitant Therapies
ITT2 Analysis Set

Therapeutic Subgroup	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Overall	169 (99.4%)	148 (85.1%)	317 (92.2%)
Agents Acting On The Renin-Angiotensin System	84 (49.4%)	76 (43.7%)	160 (46.5%)
All Other Non-Therapeutic Products	56 (32.9%)	26 (14.9%)	82 (23.8%)
All Other Therapeutic Products	58 (34.1%)	32 (18.4%)	90 (26.2%)
Analgesics	129 (75.9%)	92 (52.9%)	221 (64.2%)
Anesthetics	30 (17.6%)	18 (10.3%)	48 (14.0%)
Anti-Acne Preparations	37 (21.8%)	14 (8.0%)	51 (14.8%)
Anti-Parkinson Drugs	17 (10.0%)	6 (3.4%)	23 (6.7%)
Antianemic Preparations	47 (27.6%)	32 (18.4%)	79 (23.0%)
Antibacterials For Systemic Use	115 (67.6%)	76 (43.7%)	191 (55.5%)
Antibiotics And Chemotherapeutics For Dermatological Use	73 (42.9%)	44 (25.3%)	117 (34.0%)
Antidiarrheals, Intestinal Antiinflammatory/Antiinfective Agents	97 (57.1%)	29 (16.7%)	126 (36.6%)
Antiemetics And Antinauseants	89 (52.4%)	33 (19.0%)	122 (35.5%)
Antiepileptics	42 (24.7%)	21 (12.1%)	63 (18.3%)
Antifungals For Dermatological Use	41 (24.1%)	11 (6.3%)	52 (15.1%)
Antigout Preparations	13 (7.6%)	12 (6.9%)	25 (7.3%)
Antihemorrhagics	12 (7.1%)	7 (4.0%)	19 (5.5%)
Antihistamines For Systemic Use	91 (53.5%)	15 (8.6%)	106 (30.8%)
Antihypertensives	30 (17.6%)	8 (4.6%)	38 (11.0%)
Antiinflammatory And Antirheumatic Products	51 (30.0%)	28 (16.1%)	79 (23.0%)
Antimycotics For Systemic Use	31 (18.2%)	11 (6.3%)	42 (12.2%)
Antineoplastic Agents	14 (8.2%)	8 (4.6%)	22 (6.4%)
Antiobesity Preparations, Excl. Diet Products	7 (4.1%)	4 (2.3%)	11 (3.2%)
Antiprotozoals	30 (17.6%)	22 (12.6%)	52 (15.1%)
Antipruritics, Incl. Antihistamines, Anesthetics, Etc.	93 (54.7%)	14 (8.0%)	107 (31.1%)
Antipsoriatics	3 (1.8%)	3 (1.7%)	6 (1.7%)
Antiseptics And Disinfectants	8 (4.7%)	1 (0.6%)	9 (2.6%)

Abbreviations: ATC=anatomical therapeutic chemical; EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
Therapeutic subgroups (ATC 2nd level) are sorted alphabetically.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.5: Summary of Concomitant Therapies
ITT2 Analysis Set

Therapeutic Subgroup	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Antithrombotic Agents	118 (69.4%)	85 (48.9%)	203 (59.0%)
Antivirals For Systemic Use	12 (7.1%)	3 (1.7%)	15 (4.4%)
Appetite Stimulants	12 (7.1%)	1 (0.6%)	13 (3.8%)
Beta Blocking Agents	67 (39.4%)	59 (33.9%)	126 (36.6%)
Bile And Liver Therapy	35 (20.6%)	21 (12.1%)	56 (16.3%)
Blood Substitutes And Perfusion Solutions	99 (58.2%)	60 (34.5%)	159 (46.2%)
Calcium Channel Blockers	43 (25.3%)	45 (25.9%)	88 (25.6%)
Calcium Homeostasis	3 (1.8%)	2 (1.1%)	5 (1.5%)
Cardiac Therapy	60 (35.3%)	40 (23.0%)	100 (29.1%)
Contrast Media	9 (5.3%)	3 (1.7%)	12 (3.5%)
Corticosteroids For Systemic Use	99 (58.2%)	11 (6.3%)	110 (32.0%)
Corticosteroids, Dermatological Preparations	119 (70.0%)	15 (8.6%)	134 (39.0%)
Cough And Cold Preparations	67 (39.4%)	38 (21.8%)	105 (30.5%)
Diagnostic Agents	30 (17.6%)	17 (9.8%)	47 (13.7%)
Digestives, Incl. Enzymes	7 (4.1%)	6 (3.4%)	13 (3.8%)
Diuretics	64 (37.6%)	37 (21.3%)	101 (29.4%)
Drugs For Acid Related Disorders	101 (59.4%)	70 (40.2%)	171 (49.7%)
Drugs For Constipation	97 (57.1%)	56 (32.2%)	153 (44.5%)
Drugs For Functional Gastrointestinal Disorders	55 (32.4%)	32 (18.4%)	87 (25.3%)
Drugs For Obstructive Airway Diseases	84 (49.4%)	35 (20.1%)	119 (34.6%)
Drugs For Treatment Of Bone Diseases	2 (1.2%)	2 (1.1%)	4 (1.2%)
Drugs Used In Diabetes	60 (35.3%)	35 (20.1%)	95 (27.6%)
Ectoparasiticides, Incl. Scabicides, Insecticides And Repellents	1 (0.6%)	0	1 (0.3%)
Emollients And Protectives	55 (32.4%)	13 (7.5%)	68 (19.8%)
Endocrine Therapy	13 (7.6%)	0	13 (3.8%)
General Nutrients	28 (16.5%)	9 (5.2%)	37 (10.8%)
Gynecological Antiinfectives And Antiseptics	67 (39.4%)	42 (24.1%)	109 (31.7%)
Homeopathic Preparation	73 (42.9%)	41 (23.6%)	114 (33.1%)

Abbreviations: ATC=anatomical therapeutic chemical; EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
Therapeutic subgroups (ATC 2nd level) are sorted alphabetically.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.5: Summary of Concomitant Therapies
ITT2 Analysis Set

Therapeutic Subgroup	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Immune Sera And Immunoglobulins	3 (1.8%)	0	3 (0.9%)
Immunostimulants	14 (8.2%)	0	14 (4.1%)
Immunosuppressants	12 (7.1%)	0	12 (3.5%)
Lipid Modifying Agents	75 (44.1%)	82 (47.1%)	157 (45.6%)
Medicated Dressings	55 (32.4%)	28 (16.1%)	83 (24.1%)
Mineral Supplements	87 (51.2%)	58 (33.3%)	145 (42.2%)
Muscle Relaxants	12 (7.1%)	11 (6.3%)	23 (6.7%)
Nasal Preparations	118 (69.4%)	47 (27.0%)	165 (48.0%)
Ophthalmological And Otological Preparations	93 (54.7%)	33 (19.0%)	126 (36.6%)
Ophthalmologicals	146 (85.9%)	83 (47.7%)	229 (66.6%)
Other Alimentary Tract And Metabolism Products	46 (27.1%)	24 (13.8%)	70 (20.3%)
Other Dermatological Preparations	81 (47.6%)	51 (29.3%)	132 (38.4%)
Other Drugs For Disorders Of The Musculo-Skeletal System	7 (4.1%)	1 (0.6%)	8 (2.3%)
Other Gynecologicals	61 (35.9%)	33 (19.0%)	94 (27.3%)
Other Hematological Agents	3 (1.8%)	0	3 (0.9%)
Other Nervous System Drugs	54 (31.8%)	31 (17.8%)	85 (24.7%)
Other Respiratory System Products	7 (4.1%)	2 (1.1%)	9 (2.6%)
Otologicals	117 (68.8%)	58 (33.3%)	175 (50.9%)
Peripheral Vasodilators	3 (1.8%)	1 (0.6%)	4 (1.2%)
Pituitary And Hypothalamic Hormones And Analogues	2 (1.2%)	2 (1.1%)	4 (1.2%)
Preparations For Treatment Of Wounds And Ulcers	54 (31.8%)	26 (14.9%)	80 (23.3%)
Psychoanaleptics	38 (22.4%)	32 (18.4%)	70 (20.3%)
Psycholeptics	87 (51.2%)	53 (30.5%)	140 (40.7%)
Sex Hormones And Modulators Of The Genital System	14 (8.2%)	1 (0.6%)	15 (4.4%)
Stomatological Preparations	137 (80.6%)	77 (44.3%)	214 (62.2%)
Throat Preparations	46 (27.1%)	21 (12.1%)	67 (19.5%)
Thyroid Therapy	44 (25.9%)	19 (10.9%)	63 (18.3%)
Tonics	1 (0.6%)	4 (2.3%)	5 (1.5%)

Abbreviations: ATC=anatomical therapeutic chemical; EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
Therapeutic subgroups (ATC 2nd level) are sorted alphabetically.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.5: Summary of Concomitant Therapies
ITT2 Analysis Set

Therapeutic Subgroup	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Topical Products For Joint And Muscular Pain	90 (52.9%)	59 (33.9%)	149 (43.3%)
Unknown	3 (1.8%)	1 (0.6%)	4 (1.2%)
Unspecified Herbal And Traditional Medicine	26 (15.3%)	17 (9.8%)	43 (12.5%)
Urologicals	90 (52.9%)	55 (31.6%)	145 (42.2%)
Vaccines	3 (1.8%)	3 (1.7%)	6 (1.7%)
Vasoprotectives	101 (59.4%)	28 (16.1%)	129 (37.5%)
Vitamins	43 (25.3%)	29 (16.7%)	72 (20.9%)

Abbreviations: ATC=anatomical therapeutic chemical; EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
Therapeutic subgroups (ATC 2nd level) are sorted alphabetically.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.6.1.2: Patients With One or More Subsequent Oncologic Therapies (Considering Nivolumab in Adjuvance as Study Treatment)
ITT2 Analysis Set

Therapeutic Subgroup	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Patients in Population			
with one or more subsequent oncologic therapies	24 (14.1%)	66 (37.9%)	90 (26.2%)
with no subsequent oncologic therapies	146 (85.9%)	108 (62.1%)	254 (73.8%)
Overall	24 (14.1%)	66 (37.9%)	90 (26.2%)
Anti-PD-1 plus chemo	1 (0.6%)	1 (0.6%)	2 (0.6%)
Anti-PD-1/PD-L1	4 (2.4%)	27 (15.5%)	31 (9.0%)
Chemotherapy	16 (9.4%)	55 (31.6%)	71 (20.6%)
EV	0	9 (5.2%)	9 (2.6%)
EV plus pembro	0	1 (0.6%)	1 (0.3%)
Other	1 (0.6%)	6 (3.4%)	7 (2.0%)
Radiation Therapy	10 (5.9%)	15 (8.6%)	25 (7.3%)
Patients Who Did Not Undergo Surgery	9 (5.3%)	7 (4.0%)	16 (4.7%)
Anti-PD-1 plus chemo	0	1 (0.6%)	1 (0.3%)
Anti-PD-1/PD-L1	2 (1.2%)	0	2 (0.6%)
Chemotherapy	5 (2.9%)	5 (2.9%)	10 (2.9%)
Other	1 (0.6%)	1 (0.6%)	2 (0.6%)
Radiation Therapy	6 (3.5%)	4 (2.3%)	10 (2.9%)
Patients Who Underwent Surgery			
Overall	15 (8.8%)	59 (33.9%)	74 (21.5%)
Anti-PD-1 plus chemo	1 (0.6%)	0	1 (0.3%)
Anti-PD-1/PD-L1	2 (1.2%)	27 (15.5%)	29 (8.4%)
Chemotherapy	11 (6.5%)	50 (28.7%)	61 (17.7%)
EV	0	9 (5.2%)	9 (2.6%)

Abbreviations: ATC=anatomical therapeutic chemical; EV=enfortumab vedotin; N=number of patients; PD-1=programmed cell death protein 1; PD-L1=programmed cell death ligand 1; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
Note: The ITT2 analysis set includes all subjects that are randomized into arms B and C in stage 2.
Therapeutic subgroups (ATC 2nd level) are sorted alphabetically.
Within categories (Recurrent/Metastatic, Adjuvant or Other), therapy counts may exceed patient counts because some patients initiated multiple therapies on the same date.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.6.1.2: Patients With One or More Subsequent Oncologic Therapies (Considering Nivolumab in Adjuvance as Study Treatment)
ITT2 Analysis Set

Therapeutic Subgroup	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
EV plus pembro	0	1 (0.6%)	1 (0.3%)
Other	0	5 (2.9%)	5 (1.5%)
Radiation Therapy	4 (2.4%)	11 (6.3%)	15 (4.4%)
Recurrence/Metastatic	8 (4.7%)	46 (26.4%)	54 (15.7%)
Anti-PD-1/PD-L1	1 (0.6%)	21 (12.1%)	22 (6.4%)
Atezolizumab	0	3 (1.7%)	3 (0.9%)
Avelumab	0	9 (5.2%)	9 (2.6%)
Nivolumab	0	1 (0.6%)	1 (0.3%)
Pembrolizumab	1 (0.6%)	8 (4.6%)	9 (2.6%)
Chemotherapy	5 (2.9%)	34 (19.5%)	39 (11.3%)
EV	0	9 (5.2%)	9 (2.6%)
EV plus pembro	0	1 (0.6%)	1 (0.3%)
Other	0	3 (1.7%)	3 (0.9%)
Radiation Therapy	2 (1.2%)	11 (6.3%)	13 (3.8%)
Adjuvant	7 (4.1%)	11 (6.3%)	18 (5.2%)
Anti-PD-1 plus chemo	1 (0.6%)	0	1 (0.3%)
Anti-PD-1/PD-L1	1 (0.6%)	6 (3.4%)	7 (2.0%)
Avelumab	1 (0.6%)	0	1 (0.3%)
Nivolumab	0	5 (2.9%)	5 (1.5%)
Pembrolizumab	0	1 (0.6%)	1 (0.3%)
Chemotherapy	6 (3.5%)	3 (1.7%)	9 (2.6%)
Other	0	2 (1.1%)	2 (0.6%)
Radiation Therapy	2 (1.2%)	0	2 (0.6%)
Other	0	15 (8.6%)	15 (4.4%)
Chemotherapy	0	15 (8.6%)	15 (4.4%)

Abbreviations: ATC=anatomical therapeutic chemical; EV=enfortumab vedotin; N=number of patients; PD-1=programmed cell death protein 1; PD-L1=programmed cell death ligand 1; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
Note: The ITT2 analysis set includes all subjects that are randomized into arms B and C in stage 2.
Therapeutic subgroups (ATC 2nd level) are sorted alphabetically.
Within categories (Recurrent/Metastatic, Adjuvant or Other), therapy counts may exceed patient counts because some patients initiated multiple therapies on the same date.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.6.2.2: First Subsequent Oncologic Therapy (Considering Nivolumab in Adjuvance as Study Treatment)
ITT2 Analysis Set

Therapeutic Subgroup	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
Patients in Population			
with first subsequent oncologic therapy	24 (14.1%)	66 (37.9%)	90 (26.2%)
with no first subsequent oncologic therapy	146 (85.9%)	108 (62.1%)	254 (73.8%)
Overall	24 (14.1%)	66 (37.9%)	90 (26.2%)
Anti-PD-1 plus chemo	1 (0.6%)	1 (0.6%)	2 (0.6%)
Anti-PD-1/PD-L1	3 (1.8%)	4 (2.3%)	7 (2.0%)
Chemotherapy	14 (8.2%)	51 (29.3%)	65 (18.9%)
EV	0	1 (0.6%)	1 (0.3%)
EV plus pembro	0	1 (0.6%)	1 (0.3%)
Other	0	3 (1.7%)	3 (0.9%)
Radiation Therapy	8 (4.7%)	6 (3.4%)	14 (4.1%)
Patients Who Did Not Undergo Surgery	9 (5.3%)	7 (4.0%)	16 (4.7%)
Anti-PD-1 plus chemo	0	1 (0.6%)	1 (0.3%)
Anti-PD-1/PD-L1	2 (1.2%)	0	2 (0.6%)
Chemotherapy	5 (2.9%)	4 (2.3%)	9 (2.6%)
Other	0	1 (0.6%)	1 (0.3%)
Radiation Therapy	4 (2.4%)	2 (1.1%)	6 (1.7%)
Patients Who Underwent Surgery			
Overall	15 (8.8%)	59 (33.9%)	74 (21.5%)
Anti-PD-1 plus chemo	1 (0.6%)	0	1 (0.3%)
Anti-PD-1/PD-L1	1 (0.6%)	4 (2.3%)	5 (1.5%)
Chemotherapy	9 (5.3%)	47 (27.0%)	56 (16.3%)
EV	0	1 (0.6%)	1 (0.3%)

Abbreviations: ATC=anatomical therapeutic chemical; EV=enfortumab vedotin; N=number of patients; PD-1=programmed cell death protein 1; PD-L1=programmed cell death ligand 1; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
Note: The ITT2 analysis set includes all subjects that are randomized into arms B and C in stage 2.
Therapeutic subgroups (ATC 2nd level) are sorted alphabetically.
Within categories (Recurrent/Metastatic, Adjuvant or Other), therapy counts may exceed patient counts because some patients initiated multiple therapies on the same date.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1000.6.2.2: First Subsequent Oncologic Therapy (Considering Nivolumab in Adjuvance as Study Treatment)
ITT2 Analysis Set

Therapeutic Subgroup	EV + Pembro (N=170)	RC + PLND (N=174)	Total (N=344)
EV plus pembro	0	1 (0.6%)	1 (0.3%)
Other	0	2 (1.1%)	2 (0.6%)
Radiation Therapy	4 (2.4%)	4 (2.3%)	8 (2.3%)
Recurrence/Metastatic	8 (4.7%)	39 (22.4%)	47 (13.7%)
Anti-PD-1/PD-L1	1 (0.6%)	3 (1.7%)	4 (1.2%)
Atezolizumab	0	1 (0.6%)	1 (0.3%)
Pembrolizumab	1 (0.6%)	2 (1.1%)	3 (0.9%)
Chemotherapy	5 (2.9%)	29 (16.7%)	34 (9.9%)
EV	0	1 (0.6%)	1 (0.3%)
EV plus pembro	0	1 (0.6%)	1 (0.3%)
Other	0	1 (0.6%)	1 (0.3%)
Radiation Therapy	2 (1.2%)	4 (2.3%)	6 (1.7%)
Adjuvant	7 (4.1%)	5 (2.9%)	12 (3.5%)
Anti-PD-1 plus chemo	1 (0.6%)	0	1 (0.3%)
Anti-PD-1/PD-L1	0	1 (0.6%)	1 (0.3%)
Pembrolizumab	0	1 (0.6%)	1 (0.3%)
Chemotherapy	4 (2.4%)	3 (1.7%)	7 (2.0%)
Other	0	1 (0.6%)	1 (0.3%)
Radiation Therapy	2 (1.2%)	0	2 (0.6%)
Other	0	15 (8.6%)	15 (4.4%)
Chemotherapy	0	15 (8.6%)	15 (4.4%)

Abbreviations: ATC=anatomical therapeutic chemical; EV=enfortumab vedotin; N=number of patients; PD-1=programmed cell death protein 1; PD-L1=programmed cell death ligand 1; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
Note: The ITT2 analysis set includes all subjects that are randomized into arms B and C in stage 2.
Therapeutic subgroups (ATC 2nd level) are sorted alphabetically.
Within categories (Recurrent/Metastatic, Adjuvant or Other), therapy counts may exceed patient counts because some patients initiated multiple therapies on the same date.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Endpunkt: Gesamtüberleben (OS)

Endpunkt: Gesamtüberleben (OS); Tabellen

Table 303.1.1001.2.1: Summary of Duration of Observation Time of Overall Survival
ITT2 Analysis Set

	EV + Pembro (N=170)	RC + PLND (N=174)
Duration of observation period (months)		
n	170	174
Mean (SD)	24.1 (13.92)	20.4 (13.56)
Median	19.9	16.6
Q1 - Q3	14.3 - 36.9	11.0 - 31.6
Min - Max	1 - 52	0 - 53

Abbreviations: EV=enfortumab vedotin; Min=minimum; Max=maximum; N=number of patients; n=number of patients with non-missing values; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; Q1=first quartile; Q3=third quartile; RC=radical cystectomy; SD=standard deviation.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
The observation period for overall survival extends from the date of randomization to the last date at which endpoint data for overall survival are collected.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1003.1.1: Time to Event Analysis of Overall Survival
ITT2 Analysis Set

	EV + Pembro (N=170)	RC + PLND (N=174)	EV + Pembro vs. RC + PLND
Number of patients at risk	170 (100.0%)	174 (100.0%)	
Number of patients with events	38 (22.4%)	68 (39.1%)	
Number of patients censored	132 (77.6%)	106 (60.9%)	
Probability of being event-free (a) [95% CI] (b) at			
Month 6	94.65 [89.97, 97.18]	86.71 [80.67, 90.96]	
Month 12	86.32 [80.13, 90.69]	75.66 [68.53, 81.39]	
Month 18	80.72 [73.65, 86.06]	68.26 [60.52, 74.81]	
Month 24	79.74 [72.46, 85.29]	63.12 [54.65, 70.44]	
Month 30	76.11 [67.87, 82.51]	60.62 [51.76, 68.35]	
Month 36	74.65 [65.98, 81.42]	56.15 [46.54, 64.69]	
Month 42	70.78 [60.69, 78.73]	49.53 [38.41, 59.70]	
Month 48	70.78 [60.69, 78.73]	41.44 [27.43, 54.88]	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (c)			
50%	NC [NC, NC]	41.72 [31.84, NC]	
Difference in median			NC
Cox proportional hazards model			
Stratified HR, 95% CI			0.498 [0.334, 0.741]
Unstratified HR, 95% CI			0.499 [0.335, 0.742]
Log-rank test			
Two-sided stratified log-rank p-value			0.0004
Two-sided unstratified log-rank p-value			0.0005

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
(a) Estimated from the Kaplan-Meier Method; (b) Calculated using the log-log transformation according to Kalbfleisch and Prentice and Greenwood's formula for computing the standard error of the survival estimate; (c) Based on the Brookmeyer-Crowley Method.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
The stratification factor is tumor stage (T2N0 vs. T3/T4aN0 vs. T1-4aN1).
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1003.1.2: Type of Events and Censoring of Overall Survival
ITT2 Analysis Set

	EV + Pembro (N=170)	RC + PLND (N=174)
Number of patients at risk	170 (100.0%)	174 (100.0%)
Number of patients with events	38 (22.4%)	68 (39.1%)
Death	38 (22.4%)	68 (39.1%)
Number of patients censored	132 (77.6%)	106 (60.9%)
Censored At Last Known Alive Date	103 (60.6%)	93 (53.4%)
Censored At Data Cutoff Date	29 (17.1%)	13 (7.5%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1003.1.3: Time to Event Analysis of Overall Survival by Subgroups
ITT2 Analysis Set

Subgroup	EV + Pembro N	EV + Pembro n (%)	EV + Pembro KME [95% CI](a)	RC + PLND N	RC + PLND n (%)	RC + PLND KME [95% CI](a)	EV + Pembro vs. RC + PLND Unstratified HR [95% CI](b)	EV + Pembro vs. RC + PLND Unstratified Log-rank p-value(c)	EV + Pembro vs. RC + PLND Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	140	33 (23.6)	NC [NC, NC]	142	61 (43.0)	37.39 [26.45, NC]	0.469 [0.307, 0.716]	0.0003	0.4331
Eligible but Declined	30	5 (16.7)	NC [NC, NC]	32	7 (21.9)	NC [20.86, NC]	0.761 [0.241, 2.399]	0.6394	
Tumor Stage									
T2N0	31	4 (12.9)	NC [24.48, NC]	32	6 (18.8)	NC [NC, NC]	0.664 [0.187, 2.355]	0.5228	0.3256
T3/T4aN0	132	33 (25.0)	NC [NC, NC]	133	56 (42.1)	37.39 [26.45, NC]	0.517 [0.336, 0.796]	0.0023	
T1-4aN1	7	1 (14.3)	NC [8.54, NC]	9	6 (66.7)	10.91 [0.56, NC]	0.151 [0.018, 1.263]	0.0445	
Geographical Regions									
US	21	5 (23.8)	NC [24.48, NC]	23	9 (39.1)	NC [13.83, NC]	0.546 [0.183, 1.632]	0.2714	0.9401
EU	78	17 (21.8)	NC [41.17, NC]	77	31 (40.3)	41.72 [20.86, NC]	0.449 [0.248, 0.813]	0.0067	
MOW	71	16 (22.5)	NC [NC, NC]	74	28 (37.8)	37.39 [25.46, NC]	0.536 [0.289, 0.992]	0.0436	
Age Category									
< 65	29	2 (6.9)	NC [NC, NC]	29	12 (41.4)	NC [8.64, NC]	0.142 [0.032, 0.633]	0.0028	0.0811
>= 65	141	36 (25.5)	NC [NC, NC]	145	56 (38.6)	41.72 [26.45, NC]	0.572 [0.376, 0.871]	0.0083	
Sex									
Male	137	31 (22.6)	NC [NC, NC]	131	53 (40.5)	41.72 [31.64, NC]	0.503 [0.323, 0.784]	0.0019	0.9431
Female	33	7 (21.2)	NC [31.44, NC]	43	15 (34.9)	37.39 [18.83, NC]	0.452 [0.182, 1.119]	0.0784	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Based on 2-sided log-rank test, unadjusted for multiplicity; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

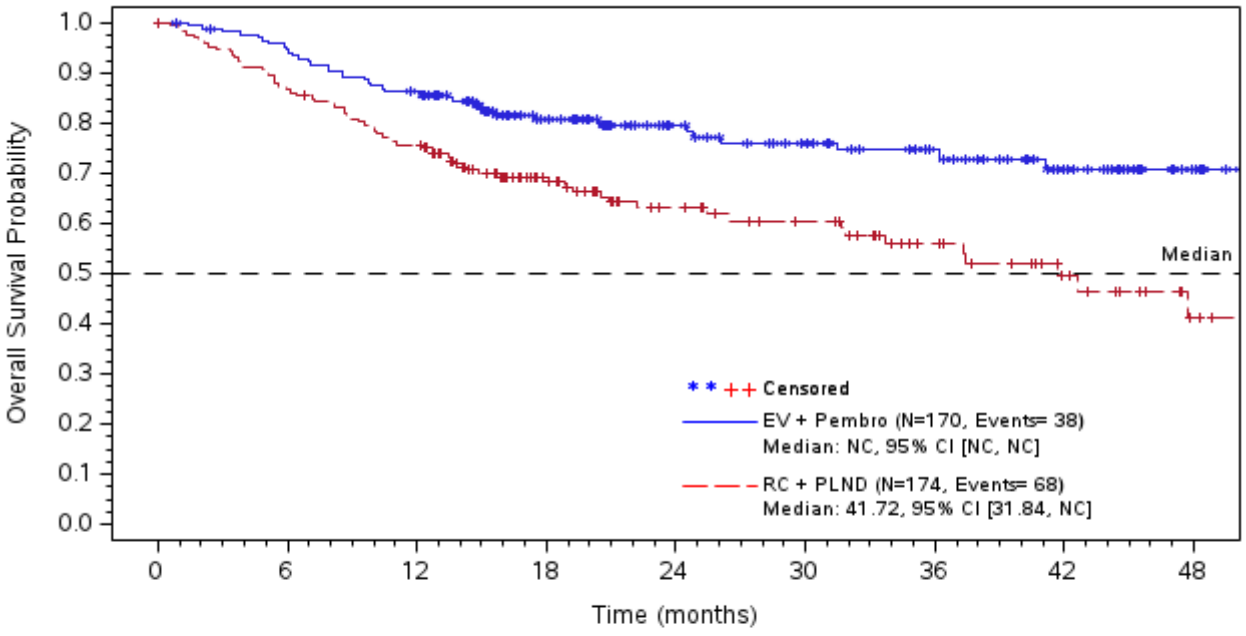
Table 303.1.1003.2.1: Time to Event Analysis of Overall Survival - Adjusted for PD-L1 Expression
ITT2 Analysis Set

	EV + Pembro (N=170)	RC + PLND (N=174)	EV + Pembro vs. RC + PLND
Number of patients at risk	170 (100.0%)	174 (100.0%)	
Number of patients with events	38 (22.4%)	68 (39.1%)	
Number of patients censored	132 (77.6%)	106 (60.9%)	
Probability of being event-free (a) [95% CI] (b) at			
Month 6	94.65 [89.97, 97.18]	86.71 [80.67, 90.96]	
Month 12	86.32 [80.13, 90.69]	75.66 [68.53, 81.39]	
Month 18	80.72 [73.65, 86.06]	68.26 [60.52, 74.81]	
Month 24	79.74 [72.46, 85.29]	63.12 [54.65, 70.44]	
Month 30	76.11 [67.87, 82.51]	60.62 [51.76, 68.35]	
Month 36	74.65 [65.98, 81.42]	56.15 [46.54, 64.69]	
Month 42	70.78 [60.69, 78.73]	49.53 [38.41, 59.70]	
Month 48	70.78 [60.69, 78.73]	41.44 [27.43, 54.88]	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (c)			
50%	NC [NC, NC]	41.72 [31.84, NC]	
Difference in median			NC
Cox proportional hazards model(d)			
Stratified HR, 95% CI			0.506 [0.340, 0.753]
Log-rank test			
Two-sided stratified log-rank p-value			0.0004

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; PD-L1=programmed cell death ligand 1; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
(a) Estimated from the Kaplan-Meier Method; (b) Calculated using the log-log transformation according to Kalbfleisch and Prentice and Greenwood's formula for computing the standard error of the survival estimate; (c) Based on the Brookmeyer-Crowley Method; (d) Adjusted for PD-L1 expression.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
The stratification factor is tumor stage (T2N0 vs. T3/T4aN0 vs. T1-4aN1).
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Endpunkt: Gesamtüberleben (OS); Abbildungen

Figure 303.1.1003.1: Kaplan-Meier Plot of Overall Survival - ITT2 Analysis Set



# at Risk (% Censored)									
1	170 (0.0)	159 (1.2)	144 (1.8)	94 (26.5)	68 (41.2)	56 (46.5)	45 (52.4)	28 (61.2)	10 (71.8)
3	174 (0.0)	150 (0.6)	130 (1.1)	75 (26.4)	54 (35.6)	45 (39.7)	30 (46.6)	18 (51.7)	6 (57.5)

Abbreviations: # at Risk=number of patients at risk; BICR=blinded independent central review; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.

Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Endpunkt: Ereignisfreies Überleben (EFS)

Endpunkt: Ereignisfreies Überleben (EFS); Tabellen

Table 303.1.1001.1.1: Summary of Duration of Observation Time of Event-free Survival (BICR) - Primary Censoring Rule
ITT2 Analysis Set

	EV + Pembro (N=170)	RC + PLND (N=174)
Duration of observation period (months)		
n	170	174
Mean (SD)	19.7 (13.64)	14.1 (12.26)
Median	15.5	11.4
Q1 - Q3	9.6 - 29.3	3.9 - 18.8
Min - Max	0 - 49	0 - 53

Abbreviations: BICR=blinded independent central review; EV=enfortumab vedotin; Min=minimum; Max=maximum; N=number of patients; n=number of patients with non-missing values; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; Q1=first quartile;
Q3=third quartile; RC=radical cystectomy; SD=standard deviation.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
The observation period for event-free survival extends from the date of randomization to the last date at which endpoint data for event-free survival are collected.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1001.1.2: Summary of Duration of Observation Time of Event-free Survival (BICR) - Sensitivity Censoring Rule 1
ITT2 Analysis Set

	EV + Pembro (N=170)	RC + PLND (N=174)
Duration of observation period (months)		
n	170	174
Mean (SD)	19.3 (13.73)	11.6 (12.19)
Median	15.5	8.8
Q1 - Q3	8.5 - 27.6	2.2 - 16.0
Min - Max	0 - 49	0 - 53

Abbreviations: BICR=blinded independent central review; EV=enfortumab vedotin; Min=minimum; Max=maximum; N=number of patients; n=number of patients with non-missing values; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; Q1=first quartile;
Q3=third quartile; RC=radical cystectomy; SD=standard deviation.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
The observation period for event-free survival extends from the date of randomization to the last date at which endpoint data for event-free survival are collected.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1001.1.3: Summary of Duration of Observation Time of Event-free Survival (BICR) - Sensitivity Censoring Rule 2
ITT2 Analysis Set

	EV + Pembro (N=170)	RC + PLND (N=174)
Duration of observation period (months)		
n	170	174
Mean (SD)	19.3 (13.73)	10.0 (12.31)
Median	15.5	4.6
Q1 - Q3	8.5 - 27.6	1.7 - 14.2
Min - Max	0 - 49	0 - 53

Abbreviations: BICR=blinded independent central review; EV=enfortumab vedotin; Min=minimum; Max=maximum; N=number of patients; n=number of patients with non-missing values; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; Q1=first quartile;
Q3=third quartile; RC=radical cystectomy; SD=standard deviation.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
The observation period for event-free survival extends from the date of randomization to the last date at which endpoint data for event-free survival are collected.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1002.1.1.1: Time to Event Analysis of Event-free Survival (BICR) - Primary Censoring Rule
ITT2 Analysis Set

	EV + Pembro (N=170)	RC + PLND (N=174)	EV + Pembro vs. RC + PLND
Number of patients at risk	170 (100.0%)	174 (100.0%)	
Number of patients with events	48 (28.2%)	95 (54.6%)	
Number of patients censored	122 (71.8%)	79 (45.4%)	
Probability of being event-free (a) [95% CI] (b) at			
Month 6	90.04 [84.25, 93.78]	70.62 [63.06, 76.92]	
Month 12	77.77 [70.42, 83.50]	55.14 [47.19, 62.38]	
Month 18	74.66 [66.92, 80.85]	47.01 [38.81, 54.77]	
Month 24	74.66 [66.92, 80.85]	39.44 [30.97, 47.78]	
Month 30	70.61 [61.84, 77.73]	38.08 [29.54, 46.56]	
Month 36	67.16 [57.42, 75.15]	35.96 [27.03, 44.96]	
Month 42	57.62 [44.96, 68.37]	32.37 [22.19, 42.95]	
Month 48	57.62 [44.96, 68.37]	28.32 [17.25, 40.42]	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (c)			
50%	NC [37.29, NC]	15.74 [10.35, 20.50]	
Difference in median			NC
Cox proportional hazards model			
Stratified HR, 95% CI			0.400 [0.282, 0.567]
Unstratified HR, 95% CI			0.399 [0.282, 0.566]
Log-rank test			
Two-sided stratified log-rank p-value			<.0001
Two-sided unstratified log-rank p-value			<.0001

Abbreviations: BICR=blinded independent central review; CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
(a) Estimated from the Kaplan-Meier Method; (b) Calculated using the log-log transformation according to Kalbfleisch and Prentice and Greenwood's formula for computing the standard error of the survival estimate; (c) Based on the Brookmeyer-Crowley Method.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
The stratification factor is tumor stage (T2N0 vs. T3/T4aN0 vs. T1-4aN1).
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1002.1.1.2: Type of Events and Censoring of Event-free Survival (BICR) - Primary Censoring Rule
ITT2 Analysis Set

	EV + Pembro (N=170)	RC + PLND (N=174)
Number of patients at risk	170 (100.0%)	174 (100.0%)
Number of patients with events	48 (28.2%)	95 (54.6%)
Patients who refused or were unable to undergo surgery	12 (7.1%)	13 (7.5%)
Radiographic disease progression precluding a curative intent surgery	5 (2.9%)	3 (1.7%)
Distant Progressive Disease	4 (2.4%)	3 (1.7%)
Locally Advanced Disease	1 (0.6%)	0 (0.0%)
Failure to undergo surgery despite residual muscle-invasive disease (MIBC)	2 (1.2%)	0 (0.0%)
Death	5 (2.9%)	10 (5.7%)
Patients who underwent surgery	36 (21.2%)	82 (47.1%)
Gross residual disease left behind at the time of surgery	2 (1.2%)	6 (3.4%)
Newly Discovered Metastatic Disease	1 (0.6%)	2 (1.1%)
Unresectable Tumor	1 (0.6%)	4 (2.3%)
Local or distant recurrence post-RC+PLND	16 (9.4%)	51 (29.3%)
Death	18 (10.6%)	25 (14.4%)
Number of patients censored	122 (71.8%)	79 (45.4%)
Patients who refused or were unable to undergo surgery	12 (7.1%)	6 (3.4%)
No Adequate Post-Baseline Disease Assessment	2 (1.2%)	3 (1.7%)
No Event Within 16 Weeks Of Last Dose Of Neoadjuvant Treatment Or Randomization	10 (5.9%)	3 (1.7%)
Patients who underwent surgery	110 (64.7%)	73 (42.0%)
No Event Before Data Cutoff	110 (64.7%)	73 (42.0%)

Abbreviations: BICR=blinded independent central review; EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
Distant Progressive Disease (PD) includes all patients who are censored at the date of PD, regardless of whether they underwent surgery afterwards or not.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1002.1.1.3: Time to Event Analysis of Event-free Survival (BICR) by Subgroups - Primary Censoring Rule
ITT2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	Unstratified HR [95% CI](b)	Unstratified Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	140	41 (29.3)	NC [37.29, NC]	142	81 (57.0)	14.23 [10.05, 20.04]	0.384 [0.263, 0.560]	<.0001	0.5633
Eligible but Declined	30	7 (23.3)	NC [13.37, NC]	32	14 (43.8)	18.73 [8.94, NC]	0.497 [0.200, 1.234]	0.1237	
Tumor Stage									
T2N0	31	5 (16.1)	NC [24.48, NC]	32	13 (40.6)	NC [7.46, NC]	0.304 [0.108, 0.857]	0.0171	0.8701
T3/T4aN0	132	40 (30.3)	NC [41.17, NC]	133	76 (57.1)	15.77 [10.22, 20.73]	0.418 [0.284, 0.613]	<.0001	
T1-4aN1	7	3 (42.9)	36.67 [8.11, NC]	9	6 (66.7)	9.46 [0.56, NC]	0.385 [0.094, 1.581]	0.1707	
Geographical Regions									
US	21	6 (28.6)	NC [24.48, NC]	23	11 (47.8)	14.32 [4.50, NC]	0.468 [0.172, 1.270]	0.1271	0.9765
EU	78	21 (26.9)	NC [36.21, NC]	77	41 (53.2)	17.15 [10.18, 41.23]	0.383 [0.226, 0.650]	0.0002	
MOW	71	21 (29.6)	NC [32.30, NC]	74	43 (58.1)	15.74 [8.94, 20.73]	0.410 [0.242, 0.693]	0.0006	
Age Category									
< 65	29	3 (10.3)	NC [NC, NC]	29	16 (55.2)	17.94 [3.52, NC]	0.135 [0.039, 0.464]	0.0002	0.0642
>= 65	141	45 (31.9)	NC [36.21, NC]	145	79 (54.5)	15.74 [10.41, 20.50]	0.451 [0.312, 0.653]	<.0001	
Sex									
Male	137	37 (27.0)	NC [41.17, NC]	131	72 (55.0)	15.74 [10.18, 20.86]	0.398 [0.268, 0.592]	<.0001	0.8648
Female	33	11 (33.3)	NC [24.84, NC]	43	23 (53.5)	18.83 [5.78, NC]	0.374 [0.177, 0.793]	0.0079	

Abbreviations: BICR=blinded independent central review; CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Based on 2-sided log-rank test, unadjusted for multiplicity; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1002.1.2.1: Time to Event Analysis of Event-free Survival (INV) - Primary Censoring Rule
ITT2 Analysis Set

	EV + Pembro (N=170)	RC + PLND (N=174)	EV + Pembro vs. RC + PLND
Number of patients at risk	170 (100.0%)	174 (100.0%)	
Number of patients with events	46 (27.1%)	98 (56.3%)	
Number of patients censored	124 (72.9%)	76 (43.7%)	
Probability of being event-free (a) [95% CI] (b) at			
Month 6	92.52 [87.19, 95.68]	72.40 [64.93, 78.55]	
Month 12	80.16 [72.99, 85.62]	56.85 [48.89, 64.04]	
Month 18	75.40 [67.57, 81.59]	46.88 [38.69, 54.63]	
Month 24	74.29 [66.23, 80.70]	38.34 [29.89, 46.72]	
Month 30	70.18 [61.14, 77.51]	34.23 [25.64, 42.98]	
Month 36	68.51 [59.02, 76.24]	32.09 [23.20, 41.30]	
Month 42	59.13 [46.66, 69.62]	32.09 [23.20, 41.30]	
Month 48	59.13 [46.66, 69.62]	14.26 [1.71, 39.35]	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (c)			
50%	NC [41.17, NC]	15.61 [11.04, 20.04]	
Difference in median			NC
Cox proportional hazards model			
Stratified HR, 95% CI			0.365 [0.256, 0.519]
Unstratified HR, 95% CI			0.362 [0.255, 0.515]
Log-rank test			
Two-sided stratified log-rank p-value			<.0001
Two-sided unstratified log-rank p-value			<.0001

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; INV=investigator; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy; SD=standard deviation.
(a) Estimated from the Kaplan-Meier Method; (b) Calculated using the log-log transformation according to Kalbfleisch and Prentice and Greenwood's formula for computing the standard error of the survival estimate; (c) Based on the Brookmeyer-Crowley Method.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
The stratification factor is tumor stage (T2N0 vs. T3/T4aN0 vs. T1-4aN1).
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1002.1.2.2: Type of Events and Censoring of Event-free Survival (INV) - Primary Censoring Rule
ITT2 Analysis Set

	EV + Pembro (N=170)	RC + PLND (N=174)
Number of patients at risk	170 (100.0%)	174 (100.0%)
Number of patients with events	46 (27.1%)	98 (56.3%)
Patients who refused or were unable to undergo surgery	9 (5.3%)	12 (6.9%)
Radiographic disease progression precluding a curative intent surgery	2 (1.2%)	3 (1.7%)
Distant Progressive Disease	2 (1.2%)	3 (1.7%)
Failure to undergo surgery despite residual muscle-invasive disease (MIBC)	2 (1.2%)	0 (0.0%)
Death	5 (2.9%)	9 (5.2%)
Patients who underwent surgery	37 (21.8%)	86 (49.4%)
Gross residual disease left behind at the time of surgery	2 (1.2%)	6 (3.4%)
Newly Discovered Metastatic Disease	1 (0.6%)	2 (1.1%)
Unresectable Tumor	1 (0.6%)	4 (2.3%)
Local or distant recurrence post-RC+PLND	17 (10.0%)	57 (32.8%)
Death	18 (10.6%)	23 (13.2%)
Number of patients censored	124 (72.9%)	76 (43.7%)
Patients who refused or were unable to undergo surgery	12 (7.1%)	6 (3.4%)
No Adequate Post-Baseline Disease Assessment	2 (1.2%)	3 (1.7%)
No Event Within 16 Weeks Of Last Dose Of Neoadjuvant Treatment Or Randomization	10 (5.9%)	3 (1.7%)
Patients who underwent surgery	112 (65.9%)	70 (40.2%)
No Event Before Data Cutoff	112 (65.9%)	70 (40.2%)

Abbreviations: EV=enfortumab vedotin; INV=investigator; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
Distant Progressive Disease (PD) includes all patients who are censored at the date of PD, regardless of whether they underwent surgery afterwards or not.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1002.2.1.1: Time to Event Analysis of Event-free Survival (BICR) - Sensitivity Censoring Rule 1
ITT2 Analysis Set

	EV + Pembro (N=170)	RC + PLND (N=174)	EV + Pembro vs. RC + PLND
Number of patients at risk	170 (100.0%)	174 (100.0%)	
Number of patients with events	36 (21.2%)	76 (43.7%)	
Number of patients censored	134 (78.8%)	98 (56.3%)	
Probability of being event-free (a) [95% CI] (b) at			
Month 6	90.06 [84.28, 93.79]	68.95 [60.71, 75.81]	
Month 12	79.97 [72.73, 85.48]	54.93 [46.31, 62.73]	
Month 18	79.19 [71.83, 84.83]	46.65 [37.62, 55.17]	
Month 24	79.19 [71.83, 84.83]	43.64 [34.32, 52.57]	
Month 30	77.72 [69.82, 83.79]	41.65 [32.03, 50.98]	
Month 36	75.68 [66.76, 82.51]	41.65 [32.03, 50.98]	
Month 42	70.76 [59.60, 79.37]	37.03 [25.18, 48.88]	
Month 48	70.76 [59.60, 79.37]	37.03 [25.18, 48.88]	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (c)			
50%	NC [NC, NC]	15.77 [10.18, 41.23]	
Difference in median			NC
Cox proportional hazards model			
Stratified HR, 95% CI			0.319 [0.213, 0.479]
Unstratified HR, 95% CI			0.331 [0.222, 0.493]
Log-rank test			
Two-sided stratified log-rank p-value			<.0001
Two-sided unstratified log-rank p-value			<.0001

Abbreviations: BICR=blinded independent central review; CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
(a) Estimated from the Kaplan-Meier Method; (b) Calculated using the log-log transformation according to Kalbfleisch and Prentice and Greenwood's formula for computing the standard error of the survival estimate; (c) Based on the Brookmeyer-Crowley Method.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
The stratification factor is tumor stage (T2N0 vs. T3/T4aN0 vs. T1-4aN1).
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1002.3.1.1: Time to Event Analysis of Event-free Survival (BICR) - Sensitivity Censoring Rule 2
ITT2 Analysis Set

	EV + Pembro (N=170)	RC + PLND (N=174)	EV + Pembro vs. RC + PLND
Number of patients at risk	170 (100.0%)	174 (100.0%)	
Number of patients with events	36 (21.2%)	71 (40.8%)	
Number of patients censored	134 (78.8%)	103 (59.2%)	
Probability of being event-free (a) [95% CI] (b) at			
Month 6	90.06 [84.28, 93.79]	66.86 [57.92, 74.32]	
Month 12	79.97 [72.73, 85.48]	50.37 [41.00, 59.01]	
Month 18	79.19 [71.83, 84.83]	43.17 [33.60, 52.37]	
Month 24	79.19 [71.83, 84.83]	40.09 [30.38, 49.59]	
Month 30	77.72 [69.82, 83.79]	38.18 [28.31, 47.96]	
Month 36	75.68 [66.76, 82.51]	38.18 [28.31, 47.96]	
Month 42	70.76 [59.60, 79.37]	33.94 [22.51, 45.70]	
Month 48	70.76 [59.60, 79.37]	33.94 [22.51, 45.70]	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (c)			
50%	NC [NC, NC]	12.71 [9.10, 20.73]	
Difference in median			NC
Cox proportional hazards model			
Stratified HR, 95% CI			0.288 [0.191, 0.434]
Unstratified HR, 95% CI			0.299 [0.200, 0.448]
Log-rank test			
Two-sided stratified log-rank p-value			<.0001
Two-sided unstratified log-rank p-value			<.0001

Abbreviations: BICR=blinded independent central review; CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
(a) Estimated from the Kaplan-Meier Method; (b) Calculated using the log-log transformation according to Kalbfleisch and Prentice and Greenwood's formula for computing the standard error of the survival estimate; (c) Based on the Brookmeyer-Crowley Method.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
The stratification factor is tumor stage (T2N0 vs. T3/T4aN0 vs. T1-4aN1).
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1002.4.1.1: Time to Event Analysis of Event-free Survival (BICR) - Primary Censoring Rule - Adjusted for PD-L1 Expression
ITT2 Analysis Set

	EV + Pembro (N=170)	RC + PLND (N=174)	EV + Pembro vs. RC + PLND
Number of patients at risk	170 (100.0%)	174 (100.0%)	
Number of patients with events	48 (28.2%)	95 (54.6%)	
Number of patients censored	122 (71.8%)	79 (45.4%)	
Probability of being event-free (a) [95% CI] (b) at			
Month 6	90.04 [84.25, 93.78]	70.62 [63.06, 76.92]	
Month 12	77.77 [70.42, 83.50]	55.14 [47.19, 62.38]	
Month 18	74.66 [66.92, 80.85]	47.01 [38.81, 54.77]	
Month 24	74.66 [66.92, 80.85]	39.44 [30.97, 47.78]	
Month 30	70.61 [61.84, 77.73]	38.08 [29.54, 46.56]	
Month 36	67.16 [57.42, 75.15]	35.96 [27.03, 44.96]	
Month 42	57.62 [44.96, 68.37]	32.37 [22.19, 42.95]	
Month 48	57.62 [44.96, 68.37]	28.32 [17.25, 40.42]	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (c)			
50%	NC [37.29, NC]	15.74 [10.35, 20.50]	
Difference in median			NC
Cox proportional hazards model(d)			
Stratified HR, 95% CI			0.391 [0.275, 0.557]
Log-rank test			
Two-sided stratified log-rank p-value			<.0001

Abbreviations: BICR=blinded independent central review; CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; PD-L1=programmed cell death ligand 1; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
(a) Estimated from the Kaplan-Meier Method; (b) Calculated using the log-log transformation according to Kalbfleisch and Prentice and Greenwood's formula for computing the standard error of the survival estimate; (c) Based on the Brookmeyer-Crowley Method; (d) Adjusted for PD-L1 expression.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
The stratification factor is tumor stage (T2N0 vs. T3/T4aN0 vs. T1-4aN1).
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1002.5.1.1: Time to Event Analysis of Event-free Survival (BICR) - Primary Censoring Rule - Censoring Deaths
ITT2 Analysis Set

	EV + Pembro (N=170)	RC + PLND (N=174)	EV + Pembro vs. RC + PLND
Number of patients at risk	170 (100.0%)	174 (100.0%)	
Number of patients with events	25 (14.7%)	60 (34.5%)	
Number of patients censored	145 (85.3%)	114 (65.5%)	
Probability of being event-free (a) [95% CI] (b) at			
Month 6	93.70 [88.60, 96.56]	80.50 [73.41, 85.87]	
Month 12	86.01 [79.33, 90.66]	66.70 [58.43, 73.70]	
Month 18	85.22 [78.39, 90.03]	61.63 [52.79, 69.30]	
Month 24	85.22 [78.39, 90.03]	55.82 [46.07, 64.49]	
Month 30	85.22 [78.39, 90.03]	55.82 [46.07, 64.49]	
Month 36	83.04 [74.63, 88.86]	55.82 [46.07, 64.49]	
Month 42	77.65 [65.97, 85.74]	50.23 [36.36, 62.59]	
Month 48	77.65 [65.97, 85.74]	50.23 [36.36, 62.59]	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (c)			
50%	NC [NC, NC]	NC [19.48, NC]	
Difference in median			NC
Cox proportional hazards model			
Stratified HR, 95% CI			0.340 [0.213, 0.544]
Log-rank test			
Two-sided stratified log-rank p-value			<.0001

Abbreviations: BICR=blinded independent central review; CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
(a) Estimated from the Kaplan-Meier Method; (b) Calculated using the log-log transformation according to Kalbfleisch and Prentice and Greenwood's formula for computing the standard error of the survival estimate; (c) Based on the Brookmeyer-Crowley Method.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
The stratification factor is tumor stage (T2N0 vs. T3/T4aN0 vs. T1-4aN1).
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

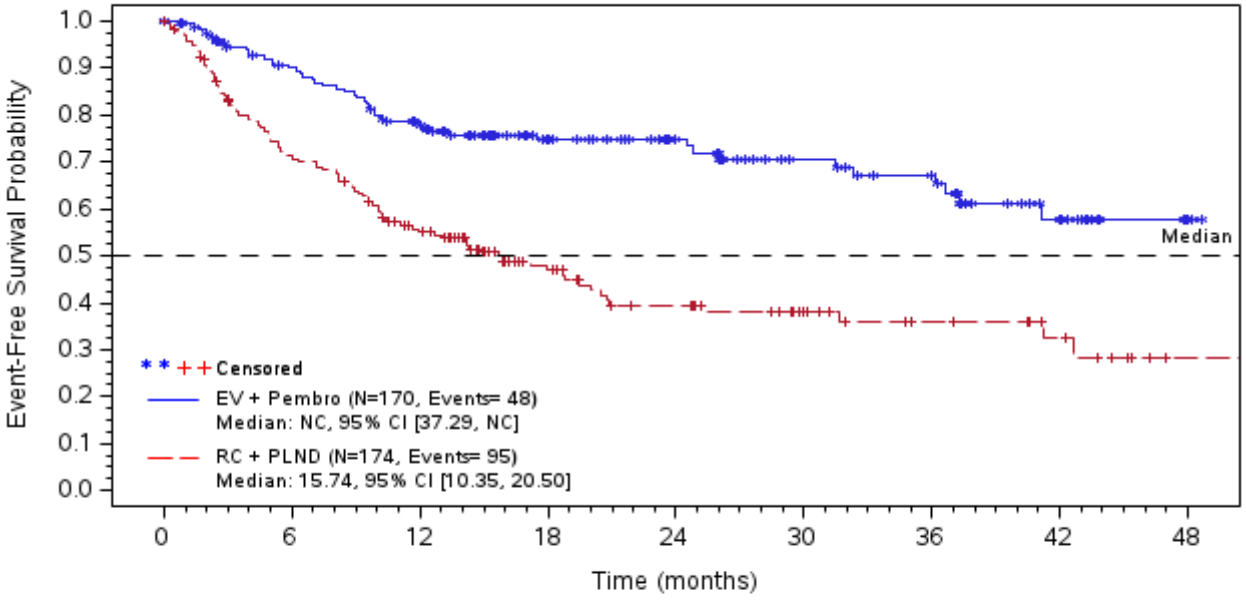
Table 303.1.1202.1.1.1: Effect Measures of Proportion of Patients with Event-free Survival Event (BICR) - Primary Censoring Rule
ITT2 Analysis Set

	EV + Pembro (N=170)	RC + PLND (N=174)	EV + Pembro vs. RC + PLND
Number of patients at risk	170 (100.0%)	174 (100.0%)	
Number of patients with events	48 (28.2%)	95 (54.6%)	
Number of patients without event	122 (71.8%)	79 (45.4%)	
Odds Ratio (a)			
Stratified OR, 95% CI			0.321 [0.204, 0.506]
Relative Risk (a)			
Stratified RR, 95% CI			0.524 [0.400, 0.688]
Risk Difference (b)			
Stratified RD, 95% CI			-0.263 [-0.362, -0.163]
Test on Differences (c)			
Stratified p-value			<.0001

Abbreviations: BICR=blinded independent central review; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
(a) Estimated using stratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Cochran-Mantel-Haenszel-adjusted absolute risk difference of EV + Pembro and RC + PLND weighted across strata; (c) Two-sided p-value based on the Cochran-Mantel-Haenszel test for treatment differences.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
The analyses were performed using tumor stage (T2N0 vs. T3/T4aN0 vs. T1-4aN1) as the stratification factor.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Endpunkt: Ereignisfreies Überleben (EFS); Abbildungen

Figure 303.1.1002.1.1: Kaplan-Meier Plot of Event-free Survival (BICR) - Primary Censoring Rule - ITT2 Analysis Set



at Risk (% Censored)

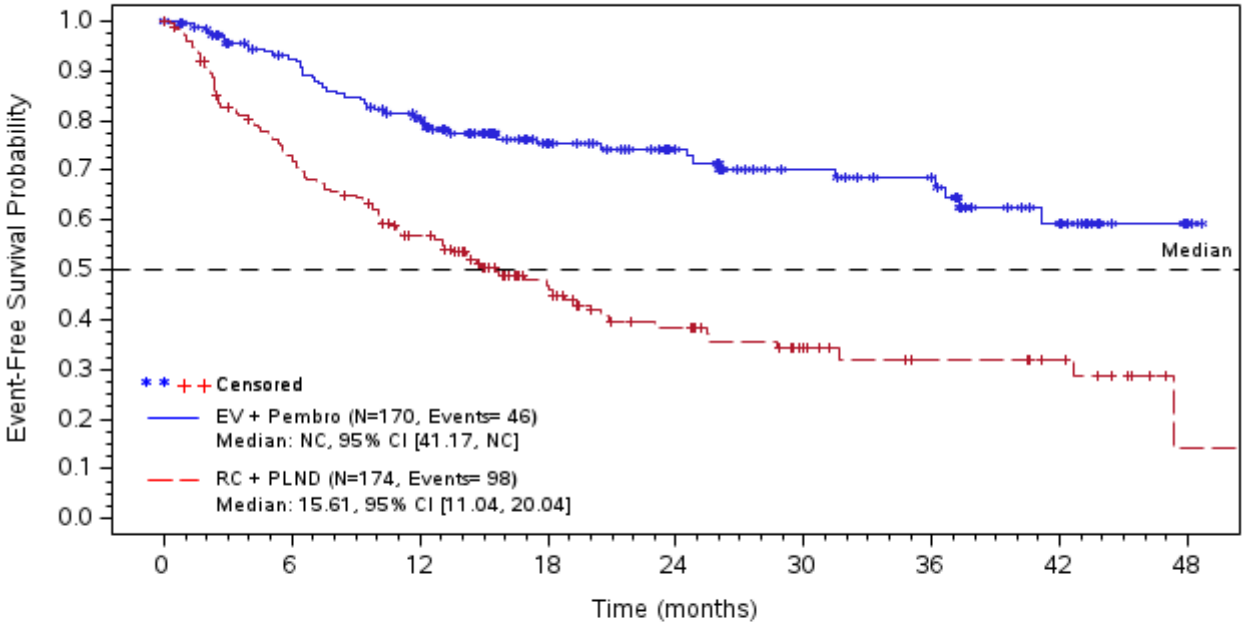
1	170 (0.0)	140 (8.2)	116 (11.2)	73 (34.1)	56 (44.1)	42 (50.6)	35 (53.5)	16 (62.4)	3 (70.0)
3	174 (0.0)	116 (5.2)	84 (9.2)	48 (24.1)	33 (28.7)	22 (34.5)	14 (38.5)	9 (40.8)	1 (44.8)

Abbreviations: # at Risk=number of patients at risk; BICR=blinded independent central review; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.

Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.1002.1.2: Kaplan-Meier Plot of Event-free Survival (INV) - Primary Censoring Rule - ITT2 Analysis Set

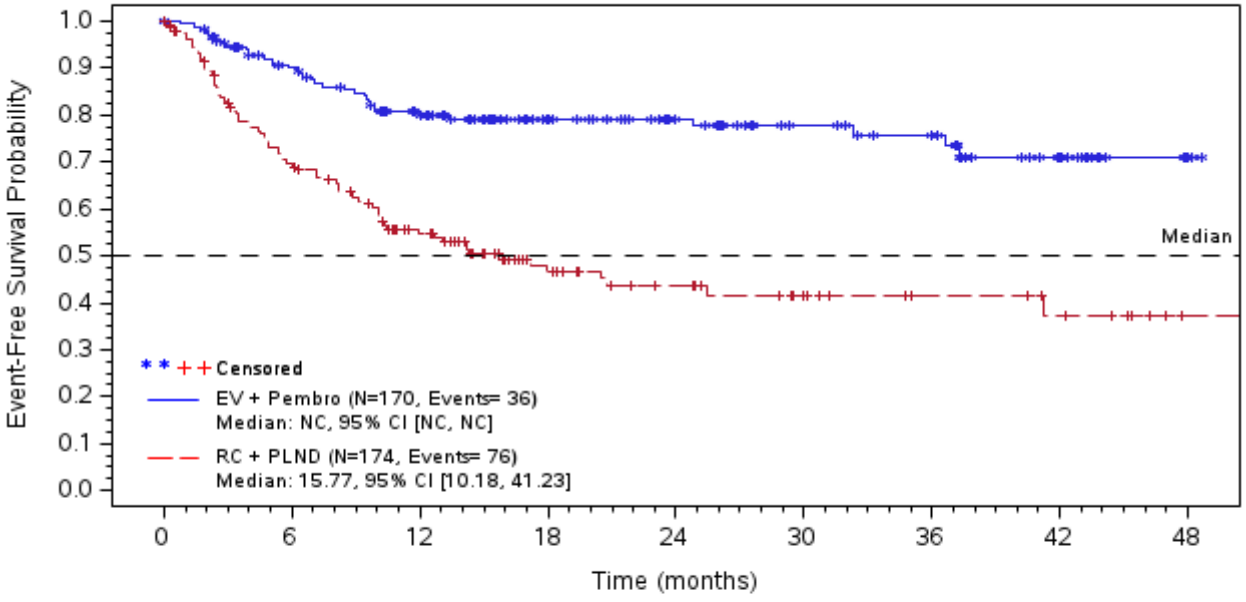


at Risk (% Censored)

1	170 (0.0)	143 (8.8)	119 (11.8)	73 (35.3)	55 (45.3)	42 (51.2)	36 (54.1)	17 (62.9)	3 (71.2)
3	174 (0.0)	118 (5.7)	86 (9.8)	49 (23.6)	32 (28.7)	20 (33.9)	13 (37.4)	10 (39.1)	1 (43.1)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; INV=investigator; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.1002.2.1: Kaplan-Meier Plot of Event-free Survival (BICR) - Sensitivity Censoring Rule 1 - ITT2 Analysis Set



at Risk (% Censored)

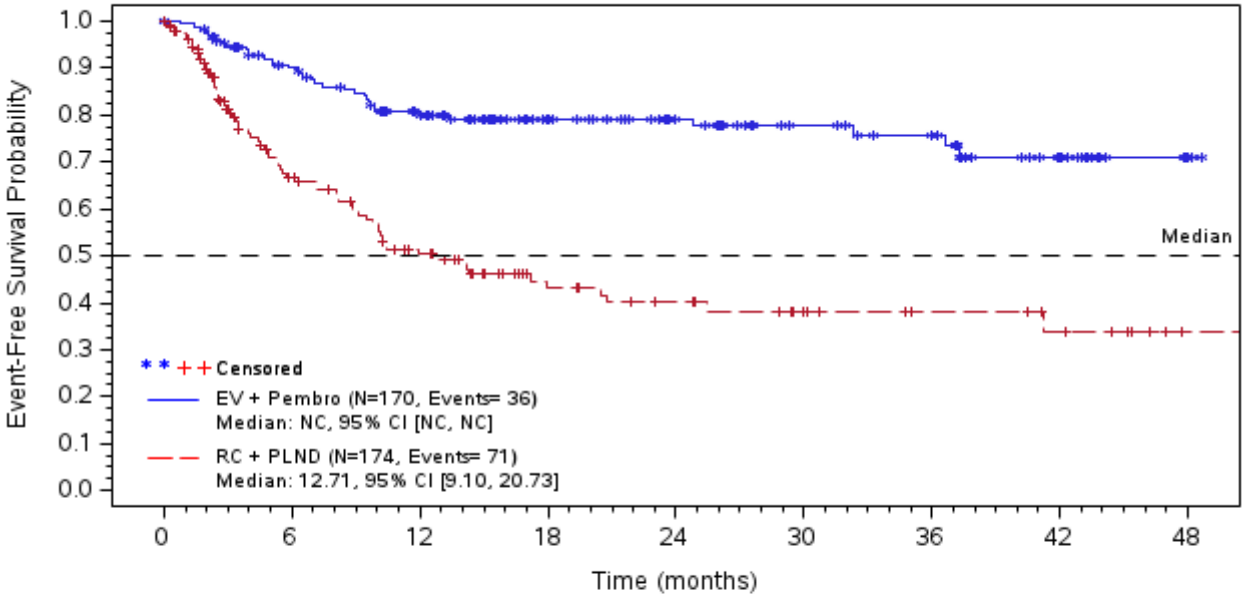
1	170 (0.0)	137 (10.0)	112 (15.9)	71 (39.4)	54 (49.4)	40 (57.1)	34 (60.0)	17 (68.8)	3 (77.1)
3	174 (0.0)	98 (17.8)	67 (24.7)	36 (37.9)	25 (43.1)	17 (47.1)	11 (50.6)	8 (51.7)	1 (55.7)

Abbreviations: # at Risk=number of patients at risk; BICR=blinded independent central review; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.

Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.1002.3.1: Kaplan-Meier Plot of Event-free Survival (BICR) - Sensitivity Censoring Rule 2 - ITT2 Analysis Set



at Risk (% Censored)

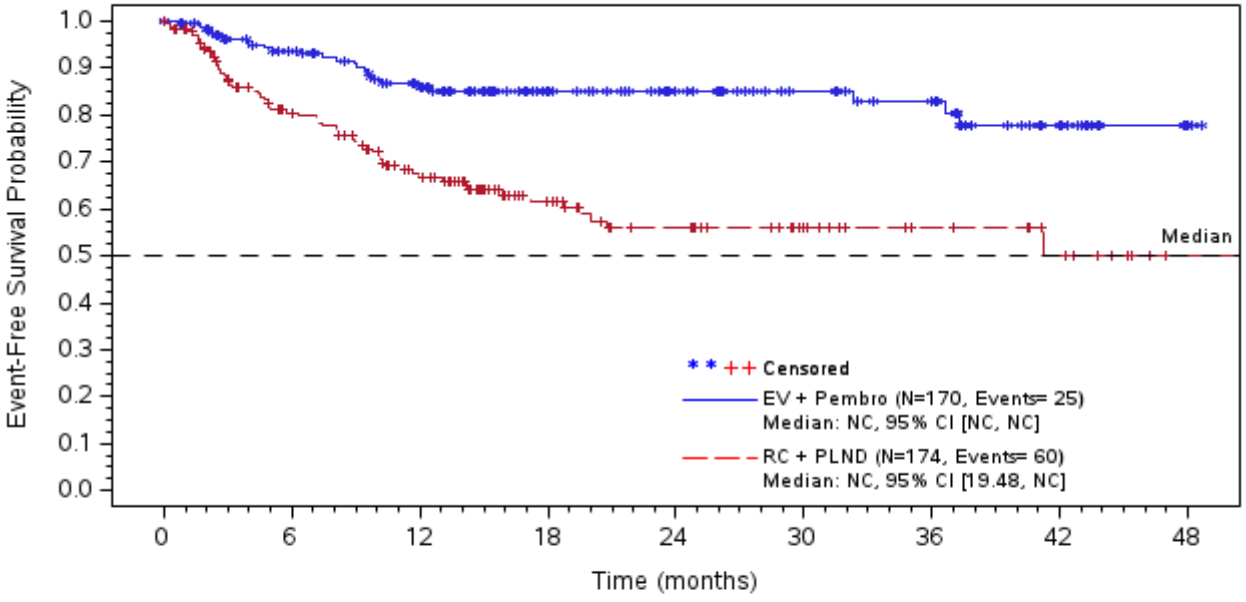
1	170 (0.0)	137 (10.0)	112 (15.9)	71 (39.4)	54 (49.4)	40 (57.1)	34 (60.0)	17 (68.8)	3 (77.1)
3	174 (0.0)	77 (31.0)	51 (35.6)	30 (44.3)	23 (47.1)	16 (50.6)	11 (53.4)	8 (54.6)	1 (58.6)

Abbreviations: # at Risk=number of patients at risk; BICR=blinded independent central review; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.

Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.1002.5.1: Kaplan-Meier Plot of Event-free Survival (BICR) - Primary Censoring Rule - Censoring Deaths - ITT2 Analysis Set



# at Risk (% Censored)									
1	170 (0.0)	140 (11.8)	116 (19.4)	73 (44.1)	56 (54.1)	42 (62.4)	35 (65.9)	16 (75.9)	3 (83.5)
3	174 (0.0)	116 (15.5)	84 (23.0)	48 (40.8)	33 (47.1)	22 (53.4)	14 (58.0)	9 (60.3)	1 (64.9)

Abbreviations: # at Risk=number of patients at risk; BICR=blinded independent central review; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.

Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Endpunkt: Krankheitsfreies Überleben (DFS)

Endpunkt: Krankheitsfreies Überleben (DFS); Tabellen

Table 303.1.1001.3.1: Summary of Duration of Observation Time of Disease-free Survival (BICR) - Primary Censoring Rule
ITT2 Analysis Set

	EV + Pembro (N=170)	RC + PLND (N=174)
Duration of observation period (months)		
n	135	129
Mean (SD)	18.8 (12.47)	14.7 (11.99)
Median	13.8	11.2
Q1 - Q3	8.3 - 32.0	6.3 - 19.6
Min - Max	1 - 44	0 - 51

Abbreviations: BICR=blinded independent central review; EV=enfortumab vedotin; Min=minimum; Max=maximum; N=number of patients; n=number of patients with non-missing values; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; Q1=first quartile;
Q3=third quartile; RC=radical cystectomy; SD=standard deviation.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
The observation period for disease-free survival extends from the datte of randomization to the last date at which endpoint data for disease-free survival are collected.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1004.1.1: Time to Event Analysis of Disease-free Survival (BICR) - Primary Censoring Rule
ITT2 Analysis Set

	EV + Pembro (N=170)	RC + PLND (N=174)	EV + Pembro vs. RC + PLND
Number of patients at risk	135 (100.0%)	129 (100.0%)	
Number of patients with events	26 (19.3%)	57 (44.2%)	
Number of patients censored	109 (80.7%)	72 (55.8%)	
Probability of being event-free (a) [95% CI] (b) at			
Month 6	88.05 [81.23, 92.50]	78.61 [70.38, 84.80]	
Month 12	84.87 [77.52, 89.97]	62.00 [52.61, 70.07]	
Month 18	84.87 [77.52, 89.97]	55.97 [46.09, 64.74]	
Month 24	83.24 [75.11, 88.90]	49.59 [39.04, 59.27]	
Month 30	81.05 [71.66, 87.59]	49.59 [39.04, 59.27]	
Month 36	73.87 [61.53, 82.79]	49.59 [39.04, 59.27]	
Month 42	69.52 [54.54, 80.42]	38.25 [22.58, 53.76]	
Month 48	NC [NC, NC]	38.25 [22.58, 53.76]	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (c)			
50%	NC [NC, NC]	23.56 [13.67, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.367 [0.231, 0.585]
Log-rank test			
Two-sided unstratified log-rank p-value			<.0001

Abbreviations: BICR=blinded independent central review; CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
(a) Estimated from the Kaplan-Meier Method; (b) Calculated using the log-log transformation according to Kalbfleisch and Prentice and Greenwood's formula for computing the standard error of the survival estimate; (c) Based on the Brookmeyer-Crowley Method.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
DFS is defined as time from surgery until recurrence or death and was determined for patients who were disease free after surgery only.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1004.1.2: Type of Events and Censoring of Disease-free Survival (BICR) - Primary Censoring Rule
ITT2 Analysis Set

	EV + Pembro (N=170)	RC + PLND (N=174)
Number of patients at risk	135 (100.0%)	129 (100.0%)
Number of patients with events	26 (19.3%)	57 (44.2%)
Death	13 (9.6%)	22 (17.1%)
Recurrence	13 (9.6%)	35 (27.1%)
Number of patients censored	109 (80.7%)	72 (55.8%)
No Event Before Data Cutoff	109 (80.7%)	72 (55.8%)

Abbreviations: BICR=blinded independent central review; EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
DFS is defined as time from surgery until recurrence or death and was determined for patients who were disease free after surgery only.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1004.1.3: Time to Event Analysis of Disease-free Survival (BICR) by Subgroups - Primary Censoring Rule
ITT2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	Unstratified HR [95% CI](b)	Unstratified Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	111	21 (18.9)	NC [NC, NC]	102	47 (46.1)	23.56 [11.47, NC]	0.343 [0.204, 0.574]	<.0001	0.4775
Eligible but Declined	24	5 (20.8)	NC [NC, NC]	27	10 (37.0)	18.37 [12.16, NC]	0.527 [0.180, 1.545]	0.2355	
Tumor Stage									
T2N0	24	2 (8.3)	NC [NC, NC]	24	9 (37.5)	NC [7.43, NC]	0.190 [0.041, 0.883]	0.0180	0.2917
T3/T4aN0	105	21 (20.0)	NC [NC, NC]	101	47 (46.5)	23.56 [13.24, NC]	0.367 [0.219, 0.615]	<.0001	
T1-4aN1	6	3 (50.0)	32.03 [4.63, NC]	4	1 (25.0)	NC [2.99, NC]	0.975 [0.087, 10.976]	0.9835	
Geographical Regions									
US	18	3 (16.7)	NC [32.03, NC]	20	8 (40.0)	NC [3.12, NC]	0.328 [0.086, 1.245]	0.0851	0.8995
EU	63	11 (17.5)	NC [37.22, NC]	58	26 (44.8)	38.77 [11.40, NC]	0.338 [0.167, 0.686]	0.0016	
MOW	54	12 (22.2)	NC [33.15, NC]	51	23 (45.1)	19.38 [12.16, NC]	0.406 [0.201, 0.820]	0.0094	
Age Category									
< 65	28	2 (7.1)	NC [NC, NC]	22	9 (40.9)	NC [7.03, NC]	0.162 [0.035, 0.753]	0.0078	0.2506
>= 65	107	24 (22.4)	NC [37.22, NC]	107	48 (44.9)	23.56 [12.16, NC]	0.410 [0.250, 0.672]	0.0003	
Sex									
Male	110	20 (18.2)	NC [NC, NC]	99	44 (44.4)	23.56 [13.24, NC]	0.364 [0.214, 0.618]	<.0001	0.9020
Female	25	6 (24.0)	NC [20.70, NC]	30	13 (43.3)	38.77 [8.08, NC]	0.368 [0.136, 0.999]	0.0421	

Abbreviations: BICR=blinded independent central review; CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Based on 2-sided log-rank test, unadjusted for multiplicity; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
DFS is defined as time from surgery until recurrence or death and was determined for patients who were disease free after surgery only.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1004.2.1: Time to Event Analysis of Disease-free Survival (BICR) - Sensitivity Analysis
ITT2 Analysis Set

	EV + Pembro (N=170)	RC + PLND (N=174)	EV + Pembro vs. RC + PLND
Number of patients at risk	170 (100.0%)	174 (100.0%)	
Number of patients with events	26 (15.3%)	57 (32.8%)	
Number of patients censored	144 (84.7%)	117 (67.2%)	
Probability of being event-free (a) [95% CI] (b) at			
Month 6	97.85 [93.49, 99.30]	86.08 [78.80, 91.00]	
Month 12	85.97 [78.88, 90.81]	67.56 [58.61, 74.99]	
Month 18	85.11 [77.86, 90.13]	59.00 [49.32, 67.45]	
Month 24	85.11 [77.86, 90.13]	51.69 [41.30, 61.12]	
Month 30	83.50 [75.49, 89.08]	49.85 [39.23, 59.57]	
Month 36	81.36 [72.12, 87.79]	49.85 [39.23, 59.57]	
Month 42	69.80 [54.98, 80.57]	44.86 [31.56, 57.29]	
Month 48	69.80 [54.98, 80.57]	39.25 [24.12, 54.07]	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (c)			
50%	NC [NC, NC]	25.46 [17.94, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.337 [0.211, 0.536]
Log-rank test			
Two-sided unstratified log-rank p-value			<.0001

Abbreviations: BICR=blinded independent central review; CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
(a) Estimated from the Kaplan-Meier Method; (b) Calculated using the log-log transformation according to Kalbfleisch and Prentice and Greenwood's formula for computing the standard error of the survival estimate; (c) Based on the Brookmeyer-Crowley Method.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
DFS is defined as time from randomization until recurrence or death and was determined for all patients in the ITT2 analysis set.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 302.3.1004.2.2: Type of Events and Censoring of Disease-free Survival (BICR) - Sensitivity Analysis
ITT2 Analysis Set

	EV + Pembro (N=170)	RC + PLND (N=174)
Number of patients at risk	170 (100.0%)	174 (100.0%)
Number of patients with events	26 (15.3%)	57 (32.8%)
Death	13 (7.6%)	22 (12.6%)
Recurrence	13 (7.6%)	35 (20.1%)
Number of patients censored	144 (84.7%)	117 (67.2%)
Patients Who Refused Or Were Unable To Undergo Surgery	21 (12.4%)	18 (10.3%)
Patients Who Underwent Surgery	123 (72.4%)	99 (56.9%)
Gross Residual Disease Left Behind At The Time Of Surgery	2 (1.2%)	6 (3.4%)
Newly Discovered Metastatic Disease	1 (0.6%)	2 (1.1%)
Unresectable Tumor	1 (0.6%)	4 (2.3%)
No Event Before Data Cutoff	109 (64.1%)	72 (41.4%)
Not Disease-Free After Surgery	12 (7.1%)	21 (12.1%)

Abbreviations: BICR=blinded independent central review; EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
DFS is defined as time from randomization until recurrence or death and was determined for all patients in the ITT2 analysis set.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1004.2.3: Time to Event Analysis of Disease-free Survival (BICR) by Subgroups - Sensitivity Analysis
ITT2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	Unstratified HR [95% CI](b)	Unstratified Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	140	21 (15.0)	NC [NC, NC]	142	47 (33.1)	25.46 [14.32, NC]	0.312 [0.186, 0.523]	<.0001	0.4380
Eligible but Declined	30	5 (16.7)	NC [NC, NC]	32	10 (31.3)	20.86 [15.77, NC]	0.496 [0.169, 1.453]	0.1917	
Tumor Stage									
T2N0	31	2 (6.5)	NC [NC, NC]	32	9 (28.1)	NC [9.53, NC]	0.181 [0.039, 0.841]	0.0141	0.2572
T3/T4aN0	132	21 (15.9)	NC [NC, NC]	133	47 (35.3)	25.46 [17.15, NC]	0.333 [0.199, 0.558]	<.0001	
T1-4aN1	7	3 (42.9)	36.67 [8.11, NC]	9	1 (11.1)	NC [9.46, NC]	1.684 [0.171, 16.535]	0.6514	
Geographical Regions									
US	21	3 (14.3)	NC [36.67, NC]	23	8 (34.8)	NC [5.39, NC]	0.306 [0.081, 1.158]	0.0649	0.8816
EU	78	11 (14.1)	NC [41.17, NC]	77	26 (33.8)	41.23 [14.16, NC]	0.311 [0.153, 0.630]	0.0006	
MOW	71	12 (16.9)	NC [37.29, NC]	74	23 (31.1)	20.73 [15.77, NC]	0.384 [0.190, 0.776]	0.0057	
Age Category									
< 65	29	2 (6.9)	NC [NC, NC]	29	9 (31.0)	NC [9.33, NC]	0.153 [0.033, 0.710]	0.0057	0.2728
>= 65	141	24 (17.0)	NC [41.17, NC]	145	48 (33.1)	25.46 [15.77, NC]	0.369 [0.225, 0.605]	<.0001	
Sex									
Male	137	20 (14.6)	NC [NC, NC]	131	44 (33.6)	25.46 [17.15, NC]	0.329 [0.194, 0.559]	<.0001	0.7963
Female	33	6 (18.2)	NC [24.84, NC]	43	13 (30.2)	41.23 [11.93, NC]	0.341 [0.125, 0.934]	0.0292	

Abbreviations: BICR=blinded independent central review; CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Based on 2-sided log-rank test, unadjusted for multiplicity; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
DFS is defined as time from randomization until recurrence or death and was determined for all patients in the ITT2 analysis set.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

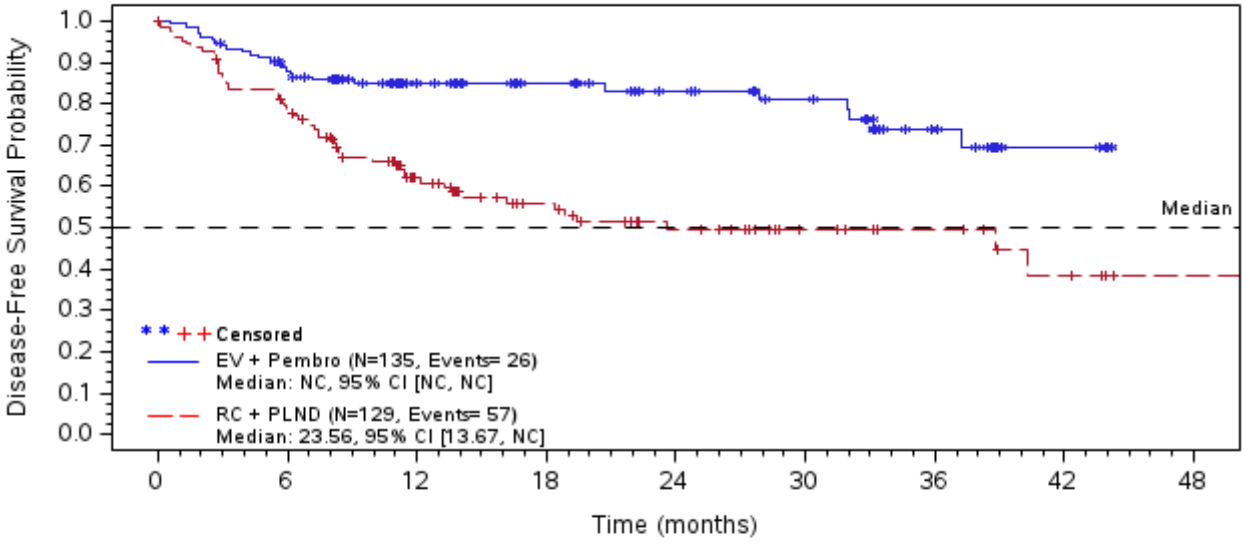
Table 303.1.1204.1.1.1: Effect Measures of Proportion of Patients with Disease-free Survival Event (BICR) - Primary Censoring Rule
ITT2 Analysis Set

	EV + Pembro (N=170)	RC + PLND (N=174)	EV + Pembro vs. RC + PLND
Number of patients at risk	135 (100.0%)	129 (100.0%)	
Number of patients with events	26 (19.3%)	57 (44.2%)	
Number of patients without event	109 (80.7%)	72 (55.8%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			0.301 [0.174, 0.523]
Relative Risk (a)			
Unstratified RR, 95% CI			0.436 [0.293, 0.648]
Risk Difference (b)			
Unstratified RD, 95% CI			-0.249 [-0.358, -0.141]
Test on Differences (c)			
Unstratified p-value			<.0001

Abbreviations: BICR=blinded independent central review; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
DFS was determined for patients who were disease free after surgery only.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Endpunkt: Krankheitsfreies Überleben (DFS); Abbildungen

Figure 303.1.1004.1: Kaplan-Meier Plot of Disease-free Survival (BICR) - Primary Censoring Rule - ITT2 Analysis Set



at Risk (% Censored)

1	135 (0.0)	115 (3.0)	75 (29.6)	58 (42.2)	43 (52.6)	36 (57.0)	18 (68.1)	5 (77.0)	0 (80.7)
3	129 (0.0)	98 (3.1)	57 (20.2)	38 (31.0)	27 (36.4)	16 (45.0)	12 (48.1)	6 (51.2)	1 (55.0)

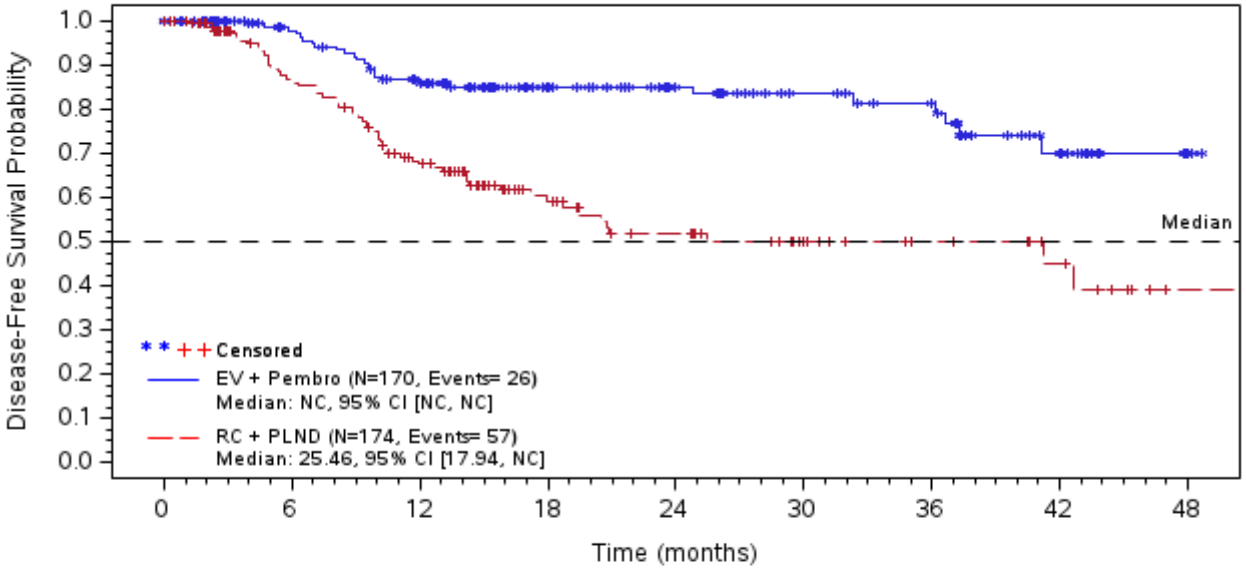
Abbreviations: # at Risk=number of patients at risk; BICR=blinded independent central review; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.

Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.

DFS is defined as time from surgery until recurrence or death and was determined for patients who were disease free after surgery only.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.1004.2: Kaplan-Meier Plot of Disease-free Survival (BICR) - Sensitivity Analysis - ITT2 Analysis Set



at Risk (% Censored)

1	170 (0.0)	133 (20.0)	111 (23.5)	70 (47.1)	53 (57.1)	41 (63.5)	35 (66.5)	16 (75.3)	3 (82.9)
3	174 (0.0)	109 (27.0)	79 (31.0)	45 (46.0)	32 (50.6)	21 (56.3)	14 (60.3)	9 (62.6)	1 (66.7)

Abbreviations: # at Risk=number of patients at risk; BICR=blinded independent central review; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.

Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.

DFS is defined as time from randomization until recurrence or death and was determined for all patients in the ITT2 analysis set.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Endpunkt: Pathologische Komplettremission (pCR)

Endpunkt: Pathologische Komplettremission (pCR); Tabellen

Table 303.1.1001.4.1: Summary of Duration of Observation Time of Pathological Complete Response (BICR)
ITT2 Analysis Set

	EV + Pembro (N=170)	RC + PLND (N=174)
Duration of observation period (months)		
n	170	174
Mean (SD)	5.2 (8.04)	4.5 (9.32)
Median	2.8	1.1
Q1 - Q3	2.6 - 3.4	0.5 - 1.7
Min - Max	0 - 52	0 - 49

Abbreviations: BICR=blinded independent central review; EV=enfortumab vedotin; Min=minimum; Max=maximum; N=number of patients; n=number of patients with non-missing values; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; Q1=first quartile;
Q3=third quartile; RC=radical cystectomy; SD=standard deviation.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
The observation period for pathological complete response extends from the date of randomization to the last date at which endpoint data for pathological complete response are collected.
Non-responder are censored at the date at which endpoint data for pathological complete response are collected. If this date is not available non-responder are censored at their last known alive date.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1005.1.1: Summary of Pathological Complete Response Rate (BICR)
ITT2 Analysis Set

	EV + Pembro (N=170)	RC + PLND (N=174)	EV + Pembro vs. RC + PLND
Number of patients at risk	170 (100.0%)	174 (100.0%)	
Number of patients with events	97 (57.1%)	15 (8.6%)	
Number of patients without event	73 (42.9%)	159 (91.4%)	
Odds Ratio (a)			
Stratified OR, 95% CI			13.520 [7.270, 25.145]
Relative Risk (a)			
Stratified RR, 95% CI			5.765 [3.534, 9.403]
Risk Difference (b)			
Stratified RD, 95% CI			0.483 [0.398, 0.569]
Test on Differences (c)			
Stratified p-value			<.0001

Abbreviations: BICR=blinded independent central review; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
(a) Estimated using stratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Cochran-Mantel-Haenszel-adjusted absolute risk difference of EV + Pembro and RC + PLND weighted across strata; (c) Two-sided p-value based on the Cochran-Mantel-Haenszel test for treatment differences.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
The stratification factor is tumor stage (T2N0 vs. T3/T4aN0 vs. T1-4aN1).
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.1005.1.2: Summary of Pathological Complete Response Rate (BICR) by Subgroups
ITT2 Analysis Set

Subgroup	EV + Pembro		RC + PLND		EV + Pembro vs. RC + PLND				
	N	n (%)	N	n (%)	Unstratified OR, 95% CI (a)	Unstratified RR, 95% CI (a)	Unstratified RD, 95% CI (b)	Difference p-value (c)	Interaction p-value (d)
Cisplatin Eligibility									
Ineligible	140	78 (55.7)	142	13 (9.2)	12.484 [6.448, 24.170]	6.086 [3.551, 10.430]	0.466 [0.371, 0.561]	<.0001	0.4692
Eligible but Declined	30	19 (63.3)	32	2 (6.3)	25.909 [5.166, 129.94]	10.133 [2.577, 39.848]	0.571 [0.379, 0.763]	<.0001	
Tumor Stage									
T2N0	31	19 (61.3)	32	6 (18.8)	6.861 [2.184, 21.554]	3.269 [1.508, 7.085]	0.425 [0.207, 0.644]	0.0006	0.1215
T3/T4aN0	132	75 (56.8)	133	9 (6.8)	18.129 [8.485, 38.734]	8.396 [4.392, 16.054]	0.501 [0.406, 0.595]	<.0001	
T1-4aN1	7	3 (42.9)	9	0 (0.0)	14.778 [0.622, 351.24]	8.750 [0.525, 145.86]	0.429 [0.062, 0.795]	0.0292	
Geographical Regions									
US	21	14 (66.7)	23	3 (13.0)	13.333 [2.930, 60.669]	5.111 [1.705, 15.319]	0.536 [0.292, 0.780]	0.0002	0.8317
EU	78	40 (51.3)	77	5 (6.5)	15.158 [5.524, 41.590]	7.897 [3.293, 18.940]	0.448 [0.324, 0.572]	<.0001	
MOW	71	43 (60.6)	74	7 (9.5)	14.699 [5.902, 36.608]	6.402 [3.087, 13.278]	0.511 [0.379, 0.643]	<.0001	
Age Category									
< 65	29	21 (72.4)	29	3 (10.3)	22.750 [5.357, 96.613]	7.000 [2.342, 20.919]	0.621 [0.424, 0.818]	<.0001	0.9079
>= 65	141	76 (53.9)	145	12 (8.3)	12.959 [6.583, 25.509]	6.513 [3.709, 11.436]	0.456 [0.363, 0.550]	<.0001	
Sex									
Male	137	81 (59.1)	131	11 (8.4)	15.779 [7.795, 31.940]	7.041 [3.933, 12.607]	0.507 [0.412, 0.602]	<.0001	0.6177
Female	33	16 (48.5)	43	4 (9.3)	9.176 [2.669, 31.548]	5.212 [1.923, 14.131]	0.392 [0.200, 0.583]	0.0001	

Abbreviations: BICR=blinded independent central review; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; n=number of patients with events; NC=not calculated; OR=odds ratio; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy; RD=risk difference; RR=relative risk.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences; (d) Type 3 likelihood ratio test p-value from binominal regression model with log-link including treatment, subgroup, and treatment x subgroup interaction.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Endpunkt: EQ-5D VAS

Endpunkt: EQ-5D VAS; Tabellen

Table 303.1.3000.2: EQ-5D-5L Visual Analog Scale - Summary of Duration of Observation Time
ITT2 Analysis Set

	EV + Pembro (N=170)	RC + PLND (N=174)
Duration of observation period (months)		
n	166	136
Mean (SD)	14.1 (9.05)	10.1 (8.59)
Median	14.3	8.8
Q1 - Q3	5.5 - 23.7	2.3 - 16.5
Min - Max	0 - 29	0 - 26

Abbreviations: EQ-5D-5L=european quality of life 5 dimensions; EV=enfortumab vedotin; Max=maxium; Min=minimum; N=number of patients; n=number of patients with non-missing values; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; Q1=first quartile; Q3=third quartile; RC=radical cystectomy; SD=standard deviation.
Note:The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
Observation time for EQ-5D-5L Visual Analog Scale questionnaire is defined as the time from randomisation until last date data were collected for EQ-5D-5L Visual Analog Scale questionnaire.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.3001.2: EQ-5D-5L Visual Analog Scale - Return Rates
ITT2 Analysis Set

Analysis Visit	EV+Pembro (N=170)			RC+PLND (N=174)		
	Compliance rate	Modified completion rate	Completion rate	Compliance rate	Modified completion rate	Completion rate
Baseline	159 / 169 (94.1%)	159 / 170 (93.5%)	159 / 170 (93.5%)	128 / 138 (92.8%)	128 / 174 (73.6%)	128 / 174 (73.6%)
Pre-surgery week 4	137 / 153 (89.5%)	137 / 170 (80.6%)	137 / 170 (80.6%)	0	0 / 174 (0.0%)	0 / 174 (0.0%)
Pre-surgery week 7	130 / 151 (86.1%)	130 / 169 (76.9%)	130 / 170 (76.5%)	0	0 / 174 (0.0%)	0 / 174 (0.0%)
Pre-surgery week 10	142 / 156 (91.0%)	142 / 168 (84.5%)	142 / 170 (83.5%)	0	0 / 174 (0.0%)	0 / 174 (0.0%)
Post-surgery week 9	126 / 142 (88.7%)	126 / 167 (75.4%)	126 / 170 (74.1%)	105 / 125 (84.0%)	105 / 166 (63.3%)	105 / 174 (60.3%)
Post-surgery week 12	86 / 101 (85.1%)	86 / 163 (52.8%)	86 / 170 (50.6%)	0	0 / 164 (0.0%)	0 / 174 (0.0%)
Post-surgery week 18	107 / 124 (86.3%)	107 / 160 (66.9%)	107 / 170 (62.9%)	79 / 89 (88.8%)	79 / 149 (53.0%)	79 / 174 (45.4%)
Post-surgery week 30	97 / 115 (84.3%)	97 / 150 (64.7%)	97 / 170 (57.1%)	68 / 81 (84.0%)	68 / 141 (48.2%)	68 / 174 (39.1%)
Post-surgery week 42	87 / 104 (83.7%)	87 / 146 (59.6%)	87 / 170 (51.2%)	58 / 72 (80.6%)	58 / 134 (43.3%)	58 / 174 (33.3%)
Post-surgery week 54	81 / 92 (88.0%)	81 / 140 (57.9%)	81 / 170 (47.6%)	48 / 57 (84.2%)	48 / 124 (38.7%)	48 / 174 (27.6%)
Post-surgery week 66	54 / 71 (76.1%)	54 / 140 (38.6%)	54 / 170 (31.8%)	35 / 44 (79.5%)	35 / 122 (28.7%)	35 / 174 (20.1%)
Post-surgery week 78	47 / 59 (79.7%)	47 / 138 (34.1%)	47 / 170 (27.6%)	24 / 30 (80.0%)	24 / 119 (20.2%)	24 / 174 (13.8%)
Post-surgery week 90	44 / 50 (88.0%)	44 / 137 (32.1%)	44 / 170 (25.9%)	25 / 27 (92.6%)	25 / 116 (21.6%)	25 / 174 (14.4%)
Post-surgery week 102	33 / 45 (73.3%)	33 / 136 (24.3%)	33 / 170 (19.4%)	19 / 24 (79.2%)	19 / 116 (16.4%)	19 / 174 (10.9%)

Abbreviations: EQ-5D-5L=european quality of life 5 dimensions 5 levels; EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
Modified completion rate is defined as the proportion of patients who completed the instrument among the ITT analysis sets while accounting for deaths.
Compliance rate is defined as the proportion of patients who completed the instrument among those who were expected to complete at a given visit
Completion rate is defined as the proportion of patients who completed the instrument among the ITT2 analysis set.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.3002.2.1.1: EQ-5D-5L - Observed Means and Change from Baseline of Visual Analog Scale
ITT2 Analysis Set

Treatment Group Analysis Visit	Value						Change from Baseline					
	n	Mean	SD	Min	Med	Max	n	Mean	SD	Min	Med	Max
EV + Pembro (N=170)												
Baseline	159	77.81	18.19	10.0	80.00	100.0						
Pre-surgery week 4	137	73.41	18.88	0.0	79.00	100.0	135	-3.84	17.78	-49.0	-1.00	60.0
Pre-surgery week 7	130	75.42	16.24	29.0	79.50	100.0	126	-2.17	20.69	-54.0	-1.00	69.0
Pre-surgery week 10	142	75.54	15.93	18.0	79.00	100.0	137	-2.18	18.91	-54.0	-2.00	66.0
Post-surgery week 9	126	71.51	18.19	5.0	70.00	100.0	122	-5.87	20.32	-53.0	-9.00	65.0
Post-surgery week 12	86	75.60	15.83	25.0	78.50	100.0	84	-2.64	21.37	-61.0	-2.00	63.0
Post-surgery week 18	107	74.24	17.69	28.0	78.00	100.0	102	-2.52	23.98	-70.0	-2.50	61.0
Post-surgery week 30	97	77.34	15.07	20.0	80.00	100.0	91	-0.64	18.51	-50.0	-1.00	51.0
Post-surgery week 42	87	76.26	14.96	40.0	80.00	100.0	82	-0.13	22.97	-56.0	-1.00	61.0
Post-surgery week 54	81	77.43	16.22	24.0	80.00	100.0	78	0.83	21.61	-66.0	0.00	64.0
Post-surgery week 66	54	76.98	14.52	45.0	79.50	98.0	53	1.94	20.31	-31.0	-1.00	51.0
Post-surgery week 78	47	78.98	16.96	4.0	81.00	100.0	46	1.39	18.28	-66.0	1.50	52.0
Post-surgery week 90	44	76.66	20.74	0.0	81.50	100.0	43	-1.19	21.41	-79.0	1.00	50.0
Post-surgery week 102	33	78.52	12.65	49.0	80.00	98.0	33	2.45	17.62	-31.0	-1.00	41.0
RC + PLND (N=174)												
Baseline	128	73.18	15.37	35.0	75.50	100.0						
Post-surgery week 9	105	68.31	18.20	20.0	69.00	100.0	100	-5.64	19.10	-68.0	-1.00	30.0
Post-surgery week 18	79	72.97	18.80	9.0	78.00	100.0	75	-0.39	20.64	-78.0	0.00	52.0
Post-surgery week 30	68	74.87	12.70	48.0	78.00	100.0	66	1.29	13.95	-34.0	0.00	45.0
Post-surgery week 42	58	77.79	13.88	38.0	79.00	100.0	55	2.75	11.12	-21.0	0.00	40.0
Post-surgery week 54	48	76.96	14.64	38.0	80.00	100.0	45	1.11	15.92	-52.0	0.00	41.0
Post-surgery week 66	35	78.40	15.00	41.0	80.00	100.0	33	3.64	14.75	-39.0	0.00	50.0
Post-surgery week 78	24	78.29	13.56	51.0	79.00	100.0	22	0.00	11.76	-15.0	0.00	35.0
Post-surgery week 90	25	80.32	13.22	50.0	82.00	99.0	22	3.32	13.79	-16.0	0.50	45.0
Post-surgery week 102	19	78.47	15.35	51.0	80.00	100.0	17	-1.65	15.56	-39.0	-2.00	24.0

Abbreviations: EQ-5D-5L=european quality of life 5 dimensions 5 levels; EV=enfortumab vedotin; Max=maximum; Med=median; Min=minimum; N=number of patients; n=number of patients with non-missing values; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy; SD=standard deviation.
Note: Baseline is the neoadjuvant cycle 1 assessment or the pre-surgery assessment if patients do not take neoadjuvant treatment.
The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.3004.2.1.1: EQ-5D-5L - Summary of Linear Mixed Model of Change from Baseline of EQ-5D Visual Analog Scale
ITT2 Analysis Set

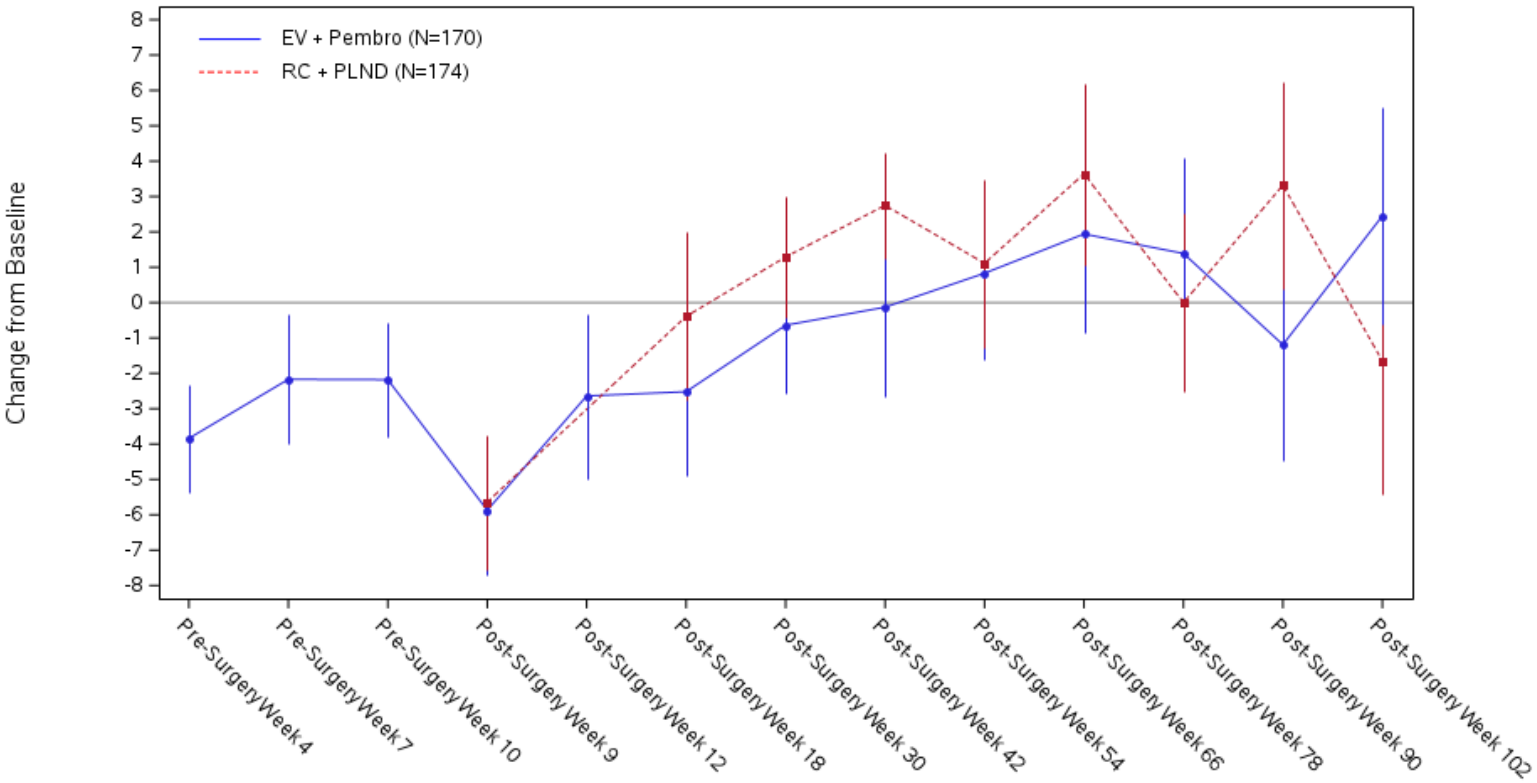
	EV + Pembro (N=170)			RC + PLND (N=174)			EV + Pembro vs. RC + PLND		
Visit	N	LS-Means SE]	95% CI for LS-Means	N	LS-Means [SE]	95% CI for LS-Means	Difference of LS-Means [SE]	95% CI for Difference	p-value
Post-surgery week 18	102	-2.85 [0.94]	[-4.71 , -0.99]	75	-3.64 [1.25]	[-6.10 , -1.19]	0.80 [1.57]	[-2.29 , 3.88]	0.6125
Overall	156	-2.42 [0.95]	[-4.30 , -0.54]	105	-2.65 [1.26]	[-5.14 , -0.17]	0.23 [1.59]	[-2.89 , 3.36]	0.8828
Hedges' g							0.02	[-0.23 , 0.27]	

Convergence Status of Linear Mixed Model:
Convergence criteria met.

Abbreviations: CI=confidence interval;EQ-5D-5L=european quality of life 5 dimensions 5 levels; EV=enfortumab vedotin; LS=least squares; MMRM=mixed model repeated measures; N=number of subjects; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy; SE=standard error.
Note: Linear mixed effects model with factors treatment, time (continuous), baseline, treatment*time as cofactors.
The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Endpunkt: EQ-5D VAS; Abbildungen

Figure 303.1.3002.2.1.1: EQ-5D-5L - Plot of Mean Change from Baseline of Visual Analog Scale
ITT2 Analysis Set



Number of patients

EV + Pembro	135	126	137	122	84	102	91	82	78	53	46	43	33
RC + PLND				100		75	66	55	45	33	22	22	17

Abbreviations: EQ-5D-5L=european quality of life 5 dimensions 5 levels; EV=enfortumab vedotin; N=number of patients;Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
Note: Baseline is the neoadjuvant cycle 1 assessment or the pre-surgery assessment if patients do not take neoadjuvant treatment.
The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Endpunkt: FACT-Bl-Cys

Endpunkt: FACT-BI-Cys; Tabellen

Table 303.1.3000.3: FACT-BL-Cys - Summary of Duration of Observation Time
ITT2 Analysis Set

	EV + Pembro (N=170)	RC + PLND (N=174)
Duration of observation period (months)		
n	166	136
Mean (SD)	14.1 (9.06)	10.1 (8.61)
Median	14.3	8.8
Q1 - Q3	5.6 - 23.7	2.3 - 16.5
Min - Max	0 - 29	0 - 26

Abbreviations: EV=enfortumab vedotin; FACT-BL-Cys=functional assessment of cancer therapy-bladder-cystectomy; Max=maxium; Min=minimum; N=number of patients; n=number of patients with non-missing values; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; Q1=first quartile; Q3=third quartile; RC=radical cystectomy; SD=standard deviation.
Note:The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
Observation time for FACT-BL-Cys questionnaire is defined as the time from randomisation until last date data were collected for FACT-BL-Cys questionnaire.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.3001.3: FACT-BL-Cys - Return Rates
ITT2 Analysis Set

Analysis Visit	EV+Pembro (N=170)			RC+PLND (N=174)		
	Compliance rate	Modified completion rate	Completion rate	Compliance rate	Modified completion rate	Completion rate
Baseline	160 / 169 (94.7%)	160 / 170 (94.1%)	160 / 170 (94.1%)	128 / 138 (92.8%)	128 / 174 (73.6%)	128 / 174 (73.6%)
Pre-surgery week 4	134 / 153 (87.6%)	134 / 170 (78.8%)	134 / 170 (78.8%)	0	0 / 174 (0.0%)	0 / 174 (0.0%)
Pre-surgery week 7	130 / 151 (86.1%)	130 / 169 (76.9%)	130 / 170 (76.5%)	0	0 / 174 (0.0%)	0 / 174 (0.0%)
Pre-surgery week 10	142 / 156 (91.0%)	142 / 168 (84.5%)	142 / 170 (83.5%)	0	0 / 174 (0.0%)	0 / 174 (0.0%)
Post-surgery week 9	125 / 142 (88.0%)	125 / 167 (74.9%)	125 / 170 (73.5%)	102 / 125 (81.6%)	102 / 166 (61.4%)	102 / 174 (58.6%)
Post-surgery week 12	84 / 101 (83.2%)	84 / 163 (51.5%)	84 / 170 (49.4%)	0	0 / 164 (0.0%)	0 / 174 (0.0%)
Post-surgery week 18	106 / 124 (85.5%)	106 / 160 (66.3%)	106 / 170 (62.4%)	79 / 89 (88.8%)	79 / 149 (53.0%)	79 / 174 (45.4%)
Post-surgery week 30	95 / 115 (82.6%)	95 / 150 (63.3%)	95 / 170 (55.9%)	68 / 81 (84.0%)	68 / 141 (48.2%)	68 / 174 (39.1%)
Post-surgery week 42	87 / 104 (83.7%)	87 / 146 (59.6%)	87 / 170 (51.2%)	57 / 72 (79.2%)	57 / 134 (42.5%)	57 / 174 (32.8%)
Post-surgery week 54	80 / 92 (87.0%)	80 / 140 (57.1%)	80 / 170 (47.1%)	48 / 57 (84.2%)	48 / 124 (38.7%)	48 / 174 (27.6%)
Post-surgery week 66	54 / 71 (76.1%)	54 / 140 (38.6%)	54 / 170 (31.8%)	35 / 44 (79.5%)	35 / 122 (28.7%)	35 / 174 (20.1%)
Post-surgery week 78	47 / 59 (79.7%)	47 / 138 (34.1%)	47 / 170 (27.6%)	24 / 30 (80.0%)	24 / 119 (20.2%)	24 / 174 (13.8%)
Post-surgery week 90	43 / 50 (86.0%)	43 / 137 (31.4%)	43 / 170 (25.3%)	25 / 27 (92.6%)	25 / 116 (21.6%)	25 / 174 (14.4%)
Post-surgery week 102	33 / 45 (73.3%)	33 / 136 (24.3%)	33 / 170 (19.4%)	19 / 24 (79.2%)	19 / 116 (16.4%)	19 / 174 (10.9%)

Abbreviations: EV=enfortumab vedotin; FACT-BL-Cys=functional assessment of cancer therapy-bladder-cystectomy; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
Modified completion rate is defined as the proportion of patients who completed the instrument among the ITT analysis sets while accounting for deaths.
Compliance rate is defined as the proportion of patients who completed the instrument among those who were expected to complete at a given visit
Completion rate is defined as the proportion of patients who completed the instrument among the ITT2 analysis set.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.3002.3.1.1: FACT-BL-Cys - Observed Means and Change from Baseline of FACT-BL-Cys Subscale
ITT2 Analysis Set

Treatment Group Analysis Visit	Value						Change from Baseline					
	n	Mean	SD	Min	Med	Max	n	Mean	SD	Min	Med	Max
EV + Pembro (N=170)												
Baseline	160	36.43	10.46	11.0	38.00	56.0						
Pre-surgery week 4	134	37.59	9.41	14.0	38.00	54.0	132	1.33	7.40	-21.0	1.00	19.0
Pre-surgery week 7	130	37.51	9.18	11.0	38.50	54.0	127	1.41	8.33	-23.0	1.00	26.0
Pre-surgery week 10	142	37.22	9.40	12.0	38.00	54.0	138	0.91	9.51	-36.0	1.00	29.0
Post-surgery week 9	125	35.24	9.39	9.0	36.00	51.0	122	-0.98	10.62	-35.0	-1.00	33.0
Post-surgery week 12	84	36.67	8.53	12.0	37.00	53.0	83	-0.63	9.96	-26.0	0.00	24.0
Post-surgery week 18	106	37.17	8.41	18.0	36.00	52.0	102	1.31	10.24	-19.0	0.00	29.0
Post-surgery week 30	95	37.79	8.52	16.0	37.00	57.0	90	0.99	9.99	-24.0	0.00	32.0
Post-surgery week 42	87	38.11	8.54	14.0	37.00	56.0	83	2.15	10.98	-32.0	2.00	25.0
Post-surgery week 54	80	37.73	8.41	23.0	36.50	56.0	78	2.00	10.89	-27.0	1.50	29.0
Post-surgery week 66	54	37.46	9.38	16.0	37.50	55.0	54	2.55	9.72	-20.0	2.50	23.0
Post-surgery week 78	47	38.15	9.34	13.0	39.00	58.0	47	2.09	10.65	-32.0	3.00	19.0
Post-surgery week 90	43	38.16	8.38	19.0	38.00	54.0	43	2.23	9.81	-23.0	1.00	22.0
Post-surgery week 102	33	38.74	8.17	21.0	38.00	54.0	33	2.77	12.93	-33.0	5.00	25.0
RC + PLND (N=174)												
Baseline	128	34.16	9.45	11.0	34.00	56.0						
Post-surgery week 9	102	33.86	8.05	12.0	35.00	55.0	97	-1.02	10.54	-29.0	-1.00	21.0
Post-surgery week 18	79	37.07	7.01	19.0	36.00	54.0	75	1.85	10.60	-26.0	2.00	24.0
Post-surgery week 30	68	38.06	6.64	24.0	38.00	56.0	66	2.67	9.17	-22.0	2.00	21.0
Post-surgery week 42	57	39.40	7.93	21.4	38.00	56.0	54	4.43	9.24	-20.0	3.57	26.0
Post-surgery week 54	48	40.04	7.82	21.0	40.00	56.0	45	4.24	9.61	-22.0	4.00	26.0
Post-surgery week 66	35	38.80	8.16	13.0	38.00	56.0	33	2.46	9.46	-20.0	2.00	25.0
Post-surgery week 78	24	38.58	6.63	25.0	37.00	52.0	22	2.87	10.90	-26.0	5.57	19.0
Post-surgery week 90	25	37.05	6.51	23.0	36.00	50.0	22	-0.90	8.95	-18.0	-1.50	24.0
Post-surgery week 102	19	38.24	7.68	22.0	38.00	52.5	17	-0.32	11.17	-18.0	-2.00	25.0

Abbreviations: EV=enfortumab vedotin; FACT-BL-Cys=functional assessment of cancer therapy-bladder-cystectomy; Max=maximum; Med=median; Min=minimum; N=number of patients; n=number of patients with non-missing values; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy; SD=standard deviation.
Note: Baseline is the neoadjuvant cycle 1 assessment or the pre-surgery assessment if patients do not take neoadjuvant treatment.
The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.3002.3.2.1: FACT-BL-Cys - Observed Means and Change from Baseline of FACT-BL-Cys Total Score
ITT2 Analysis Set

Treatment Group Analysis Visit	Value						Change from Baseline					
	n	Mean	SD	Min	Med	Max	n	Mean	SD	Min	Med	Max
EV + Pembro (N=170)												
Baseline	160	118.22	24.22	46.7	122.00	164.0						
Pre-surgery week 4	134	115.91	23.05	61.7	116.50	157.0	132	-1.40	18.36	-66.0	-1.08	58.0
Pre-surgery week 7	130	116.37	22.11	68.2	118.33	156.0	127	-2.23	17.94	-73.0	-3.00	47.0
Pre-surgery week 10	142	114.65	23.71	53.0	115.00	160.0	138	-3.32	21.32	-86.0	-2.82	54.0
Post-surgery week 9	125	109.46	25.10	34.8	110.00	151.0	122	-8.38	22.45	-80.0	-5.08	41.0
Post-surgery week 12	84	113.70	23.50	61.0	115.92	159.0	83	-6.99	23.01	-68.7	-4.50	43.8
Post-surgery week 18	106	115.12	24.33	50.0	115.50	158.0	102	-1.42	24.95	-58.7	-2.67	54.5
Post-surgery week 30	95	117.80	23.26	58.0	120.00	159.0	90	-1.53	22.22	-66.0	-0.75	82.3
Post-surgery week 42	87	117.39	23.03	68.5	119.00	159.0	83	0.48	25.80	-80.0	-0.83	74.5
Post-surgery week 54	80	117.15	25.07	65.0	115.50	159.0	78	-0.41	25.12	-71.7	0.00	59.3
Post-surgery week 66	54	118.70	23.37	70.2	117.00	158.0	54	3.59	22.21	-54.7	3.43	59.5
Post-surgery week 78	47	116.15	25.21	58.0	118.00	159.0	47	-0.43	23.79	-59.7	3.50	59.0
Post-surgery week 90	43	117.95	25.50	66.0	119.33	162.0	43	0.89	23.28	-67.7	-0.33	53.2
Post-surgery week 102	33	118.83	21.82	61.0	122.00	160.0	33	1.38	26.13	-58.7	4.88	50.0
RC + PLND (N=174)												
Baseline	128	111.44	21.58	42.0	114.00	164.0						
Post-surgery week 9	102	107.49	22.01	58.0	109.25	153.0	97	-6.96	20.80	-69.2	-6.50	40.0
Post-surgery week 18	79	114.05	18.83	68.0	111.33	158.5	75	-0.99	20.20	-53.0	1.00	43.5
Post-surgery week 30	68	115.56	19.60	73.0	114.00	162.0	66	-0.07	17.36	-46.0	0.92	32.5
Post-surgery week 42	57	121.52	20.72	74.4	122.83	164.0	54	5.28	17.08	-29.0	2.50	54.0
Post-surgery week 54	48	121.61	22.70	60.0	120.75	164.0	45	3.57	16.96	-40.7	7.00	31.0
Post-surgery week 66	35	120.54	24.11	38.0	120.00	163.0	33	1.83	16.33	-37.0	1.83	27.3
Post-surgery week 78	24	120.11	19.20	85.7	118.00	160.0	22	0.14	17.53	-37.0	2.83	23.5
Post-surgery week 90	25	115.86	21.98	65.0	119.00	145.3	22	-3.57	17.40	-53.7	-2.50	28.5
Post-surgery week 102	19	123.41	19.42	81.5	121.00	156.5	17	-1.38	19.44	-37.2	0.00	32.8

Abbreviations: EV=enfortumab vedotin; FACT-BL-Cys=functional assessment of cancer therapy-bladder-cystectomy; Max=maximum; Med=median; Min=minimum; N=number of patients; n=number of patients with non-missing values; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy; SD=standard deviation.
Note: Baseline is the neoadjuvant cycle 1 assessment or the pre-surgery assessment if patients do not take neoadjuvant treatment.
The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.3002.3.3.1: FACT-BL-Cys - Observed Means and Change from Baseline of FACT-G Total Score
ITT2 Analysis Set

Treatment Group Analysis Visit	Value						Change from Baseline					
	n	Mean	SD	Min	Med	Max	n	Mean	SD	Min	Med	Max
EV + Pembro (N=170)												
Baseline	160	81.79	15.75	34.7	85.00	108.0						
Pre-surgery week 4	134	78.31	15.80	35.7	80.00	106.0	132	-2.73	14.20	-51.0	-3.00	51.0
Pre-surgery week 7	130	78.86	14.65	41.2	79.50	105.0	127	-3.64	12.29	-50.0	-3.00	27.8
Pre-surgery week 10	142	77.43	16.57	30.0	77.92	108.0	138	-4.23	15.01	-50.0	-2.58	41.0
Post-surgery week 9	125	74.22	17.46	25.8	76.17	103.0	122	-7.40	15.86	-50.2	-5.83	41.8
Post-surgery week 12	84	77.02	16.56	33.0	80.00	107.0	83	-6.36	15.62	-45.0	-5.00	24.8
Post-surgery week 18	106	77.94	17.40	29.0	79.92	106.0	102	-2.73	17.75	-39.7	-2.25	38.3
Post-surgery week 30	95	80.01	16.34	34.7	83.00	107.0	90	-2.52	15.17	-42.0	-0.50	50.3
Post-surgery week 42	87	79.28	15.82	37.5	81.00	107.0	83	-1.68	17.36	-50.0	0.00	50.5
Post-surgery week 54	80	79.42	18.15	39.7	79.00	107.0	78	-2.40	17.74	-56.3	-0.08	44.3
Post-surgery week 66	54	81.24	14.99	50.2	81.58	105.0	54	1.04	16.18	-37.2	1.08	46.5
Post-surgery week 78	47	78.00	16.96	39.7	80.00	106.0	47	-2.51	16.13	-40.7	-1.00	44.0
Post-surgery week 90	43	79.79	17.97	39.3	82.00	108.0	43	-1.34	16.14	-44.7	-0.83	42.0
Post-surgery week 102	33	80.10	15.51	40.0	80.67	106.0	33	-1.38	16.38	-38.7	1.17	40.0
RC + PLND (N=174)												
Baseline	128	77.28	15.06	30.0	78.83	108.0						
Post-surgery week 9	102	73.63	16.08	35.2	75.00	104.0	97	-5.93	14.42	-52.2	-4.83	28.0
Post-surgery week 18	79	76.98	14.61	41.0	79.00	106.8	75	-2.84	14.19	-45.0	-1.00	24.5
Post-surgery week 30	68	77.50	14.53	41.0	76.92	106.0	66	-2.74	13.00	-51.0	-1.00	19.0
Post-surgery week 42	57	82.12	14.22	47.7	83.00	108.0	54	0.84	12.23	-34.0	1.83	28.0
Post-surgery week 54	48	81.57	16.71	37.0	83.92	108.0	45	-0.68	13.57	-40.0	3.00	19.0
Post-surgery week 66	35	81.74	17.53	25.0	81.00	108.0	33	-0.63	11.11	-29.0	1.00	16.0
Post-surgery week 78	24	81.53	14.32	53.7	82.00	108.0	22	-2.73	9.64	-23.0	1.33	8.0
Post-surgery week 90	25	78.81	17.57	38.0	81.00	104.0	22	-2.67	12.16	-41.7	-0.50	17.0
Post-surgery week 102	19	85.18	13.57	59.5	82.00	106.0	17	-1.06	11.99	-24.2	2.00	21.8

Abbreviations: EV=enfortumab vedotin; FACT-BL-Cys=functional assessment of cancer therapy-bladder-cystectomy; Max=maximum; Med=median; Min=minimum; N=number of patients; n=number of patients with non-missing values; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy; SD=standard deviation.
Note: Baseline is the neoadjuvant cycle 1 assessment or the pre-surgery assessment if patients do not take neoadjuvant treatment.
The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.3002.3.4.1: FACT-BL-Cys - Observed Means and Change from Baseline of Emotional Well-Being
ITT2 Analysis Set

Treatment Group Analysis Visit	Value						Change from Baseline					
	n	Mean	SD	Min	Med	Max	n	Mean	SD	Min	Med	Max
EV + Pembro (N=170)												
Baseline	160	17.65	4.55	0.0	19.00	24.0						
Pre-surgery week 4	134	17.90	4.31	5.0	19.00	24.0	132	0.22	3.62	-9.0	0.00	10.0
Pre-surgery week 7	130	18.11	4.41	6.0	19.00	24.0	127	0.32	4.08	-13.0	0.00	16.0
Pre-surgery week 10	142	17.62	4.87	0.0	19.00	24.0	138	0.04	4.31	-12.0	0.00	13.0
Post-surgery week 9	125	18.02	4.76	2.0	19.00	24.0	122	0.37	4.14	-11.0	1.00	15.0
Post-surgery week 12	84	18.04	4.59	4.0	19.00	24.0	83	-0.40	4.59	-18.0	0.00	10.0
Post-surgery week 18	106	18.44	4.83	1.0	19.00	24.0	102	1.08	4.98	-12.0	1.00	20.0
Post-surgery week 30	95	18.67	4.96	3.0	20.00	24.0	90	1.18	4.60	-12.0	1.00	17.0
Post-surgery week 42	87	18.78	4.35	6.0	20.00	24.0	83	1.18	4.25	-14.0	1.00	20.0
Post-surgery week 54	80	17.95	5.04	6.0	19.00	24.0	78	0.60	4.89	-14.0	1.00	20.0
Post-surgery week 66	54	19.02	4.01	7.0	20.00	24.0	54	1.28	4.53	-9.0	1.00	19.0
Post-surgery week 78	47	18.34	4.65	1.0	19.00	24.0	47	0.68	5.29	-11.0	0.00	20.0
Post-surgery week 90	43	18.23	5.21	4.0	20.00	24.0	43	-0.02	4.18	-14.0	0.00	9.0
Post-surgery week 102	33	18.15	4.73	6.0	19.00	24.0	33	0.03	4.88	-12.0	0.00	9.0
RC + PLND (N=174)												
Baseline	128	17.11	4.60	1.0	18.00	24.0						
Post-surgery week 9	102	17.77	4.52	1.0	18.00	24.0	97	0.41	4.01	-13.0	0.00	10.0
Post-surgery week 18	79	17.97	4.05	6.0	19.00	24.0	75	0.57	3.69	-8.0	0.00	10.0
Post-surgery week 30	68	18.35	3.74	8.0	19.00	24.0	66	0.62	3.93	-7.0	0.00	14.0
Post-surgery week 42	57	19.39	3.38	11.0	20.00	24.0	54	1.46	3.55	-4.0	0.50	11.0
Post-surgery week 54	48	19.38	3.75	9.0	20.00	24.0	45	1.60	3.85	-8.0	1.00	14.0
Post-surgery week 66	35	19.23	3.73	9.0	19.00	24.0	33	1.82	3.61	-5.0	2.00	12.0
Post-surgery week 78	24	19.00	2.47	12.0	19.00	24.0	22	1.36	2.75	-3.0	1.00	9.0
Post-surgery week 90	25	17.72	4.97	3.0	19.00	24.0	22	0.64	5.26	-14.0	1.00	13.0
Post-surgery week 102	19	18.89	2.66	13.0	20.00	24.0	17	1.24	3.65	-4.0	1.00	11.0

Abbreviations: EV=enfortumab vedotin; FACT-BL-Cys=functional assessment of cancer therapy-bladder-cystectomy; Max=maximum; Med=median; Min=minimum; N=number of patients; n=number of patients with non-missing values; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy; SD=standard deviation.
Note: Baseline is the neoadjuvant cycle 1 assessment or the pre-surgery assessment if patients do not take neoadjuvant treatment.
The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.3002.3.5.1: FACT-BL-Cys - Observed Means and Change from Baseline of Functional Well-Being
ITT2 Analysis Set

Treatment Group Analysis Visit	Value						Change from Baseline					
	n	Mean	SD	Min	Med	Max	n	Mean	SD	Min	Med	Max
EV + Pembro (N=170)												
Baseline	160	18.41	6.27	0.0	19.00	28.0						
Pre-surgery week 4	134	16.81	6.49	0.0	17.00	28.0	132	-1.40	6.96	-28.0	-1.00	24.0
Pre-surgery week 7	130	17.60	5.37	2.0	17.50	28.0	127	-0.93	5.51	-22.0	-1.00	16.0
Pre-surgery week 10	142	17.25	5.97	0.0	17.50	28.0	138	-1.12	5.68	-21.0	-1.00	17.0
Post-surgery week 9	125	14.86	6.15	1.0	15.00	28.0	122	-3.48	6.25	-25.0	-3.00	15.0
Post-surgery week 12	84	16.77	5.18	5.0	17.50	28.0	83	-2.22	5.99	-18.0	-2.00	11.0
Post-surgery week 18	106	16.94	6.21	1.0	18.00	28.0	102	-1.25	7.15	-25.0	-1.50	18.0
Post-surgery week 30	95	17.73	5.78	4.0	18.00	28.0	90	-1.24	5.54	-16.0	-1.00	18.0
Post-surgery week 42	87	17.66	5.98	0.0	18.00	28.0	83	-0.67	7.16	-27.0	-1.00	20.0
Post-surgery week 54	80	18.09	6.34	4.0	18.00	28.0	78	-0.96	7.00	-22.0	-0.50	15.0
Post-surgery week 66	54	18.28	5.29	6.0	17.50	28.0	54	0.41	5.83	-14.0	0.00	12.0
Post-surgery week 78	47	17.23	5.94	0.0	17.00	28.0	47	-1.04	5.02	-13.0	0.00	15.0
Post-surgery week 90	43	17.77	5.66	7.0	17.00	28.0	43	-0.42	5.41	-11.0	-1.00	14.0
Post-surgery week 102	33	17.85	6.27	2.0	18.00	28.0	33	-0.33	6.87	-19.0	1.00	13.0
RC + PLND (N=174)												
Baseline	128	16.73	6.21	0.0	17.00	28.0						
Post-surgery week 9	102	14.33	6.59	0.0	14.00	28.0	97	-3.38	6.57	-24.0	-3.00	10.0
Post-surgery week 18	79	16.29	6.32	0.0	17.00	28.0	75	-1.41	6.45	-28.0	0.00	10.0
Post-surgery week 30	68	16.88	5.99	2.0	17.00	28.0	66	-1.11	6.43	-23.0	0.00	13.0
Post-surgery week 42	57	18.88	5.52	6.0	19.00	28.0	54	0.46	4.51	-10.0	1.00	10.0
Post-surgery week 54	48	18.31	6.06	7.0	20.00	28.0	45	-0.44	5.16	-14.0	0.00	16.0
Post-surgery week 66	35	19.00	6.30	4.0	19.00	28.0	33	-0.18	4.66	-13.0	0.00	9.0
Post-surgery week 78	24	18.08	6.18	8.0	19.00	28.0	22	-1.27	4.38	-11.0	0.00	4.0
Post-surgery week 90	25	17.88	5.72	3.0	18.00	28.0	22	-0.95	5.37	-13.0	0.00	8.0
Post-surgery week 102	19	20.00	6.11	8.0	20.00	28.0	17	0.29	4.70	-8.0	1.00	10.0

Abbreviations: EV=enfortumab vedotin; FACT-BL-Cys=functional assessment of cancer therapy-bladder-cystectomy; Max=maximum; Med=median; Min=minimum; N=number of patients; n=number of patients with non-missing values; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy; SD=standard deviation.
Note: Baseline is the neoadjuvant cycle 1 assessment or the pre-surgery assessment if patients do not take neoadjuvant treatment.
The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.3002.3.6.1: FACT-BL-Cys - Observed Means and Change from Baseline of Physical Well-Being
ITT2 Analysis Set

Treatment Group Analysis Visit	Value						Change from Baseline					
	n	Mean	SD	Min	Med	Max	n	Mean	SD	Min	Med	Max
EV + Pembro (N=170)												
Baseline	160	24.26	3.95	9.0	26.00	28.0						
Pre-surgery week 4	134	22.54	4.77	6.0	24.00	28.0	132	-1.45	3.98	-14.0	-1.00	7.0
Pre-surgery week 7	130	21.61	5.13	0.0	23.00	28.0	127	-2.67	5.02	-28.0	-2.00	12.0
Pre-surgery week 10	142	22.01	4.88	8.0	23.00	28.0	138	-2.14	4.86	-18.0	-2.00	18.0
Post-surgery week 9	125	21.09	5.60	2.0	22.00	28.0	122	-3.17	5.06	-19.0	-2.00	8.0
Post-surgery week 12	84	21.75	5.56	2.0	23.00	28.0	83	-2.49	5.67	-19.0	-1.00	10.0
Post-surgery week 18	106	22.23	5.29	6.0	24.00	28.0	102	-1.95	5.68	-18.0	-1.00	11.0
Post-surgery week 30	95	23.19	4.15	13.0	24.00	28.0	90	-1.26	4.58	-15.0	-1.00	11.0
Post-surgery week 42	87	22.90	4.17	9.0	24.00	28.0	83	-1.14	4.91	-16.0	-1.00	13.0
Post-surgery week 54	80	22.75	4.63	10.0	24.00	28.0	78	-1.36	4.79	-18.0	-1.00	10.0
Post-surgery week 66	54	23.37	3.88	11.0	24.50	28.0	54	-0.19	3.95	-10.0	0.00	13.0
Post-surgery week 78	47	23.45	4.68	7.0	25.00	28.0	47	-0.43	3.79	-12.0	0.00	6.0
Post-surgery week 90	43	22.93	5.04	9.0	25.00	28.0	43	-0.86	4.19	-16.0	0.00	7.0
Post-surgery week 102	33	23.76	3.84	15.0	25.00	28.0	33	0.12	3.99	-12.0	0.00	7.0
RC + PLND (N=174)												
Baseline	128	23.20	4.72	5.0	24.00	28.0						
Post-surgery week 9	102	21.18	4.83	9.0	21.50	28.0	97	-2.35	5.25	-19.0	-2.00	17.0
Post-surgery week 18	79	23.11	4.41	7.0	24.00	28.0	75	-1.01	4.16	-16.0	-1.00	8.0
Post-surgery week 30	68	23.90	3.82	13.0	25.00	28.0	66	-0.30	3.55	-11.0	0.00	12.0
Post-surgery week 42	57	23.96	3.63	12.0	25.00	28.0	54	-0.22	3.22	-7.0	0.00	10.0
Post-surgery week 54	48	24.15	4.56	8.0	26.00	28.0	45	-0.78	4.11	-15.0	0.00	11.0
Post-surgery week 66	35	23.69	4.40	12.0	25.00	28.0	33	-0.88	2.91	-8.0	0.00	4.0
Post-surgery week 78	24	23.67	4.27	12.0	24.50	28.0	22	-0.86	2.96	-9.0	0.00	4.0
Post-surgery week 90	25	23.24	4.46	11.0	25.00	28.0	22	-0.68	3.01	-10.0	-0.50	4.0
Post-surgery week 102	19	24.16	4.06	14.0	26.00	28.0	17	-0.82	3.78	-11.0	0.00	4.0

Abbreviations: EV=enfortumab vedotin; FACT-BL-Cys=functional assessment of cancer therapy-bladder-cystectomy; Max=maximum; Med=median; Min=minimum; N=number of patients; n=number of patients with non-missing values; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy; SD=standard deviation.
Note: Baseline is the neoadjuvant cycle 1 assessment or the pre-surgery assessment if patients do not take neoadjuvant treatment.
The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.3002.3.7.1: FACT-BL-Cys - Observed Means and Change from Baseline of Social/Family Well-Being
ITT2 Analysis Set

Treatment Group Analysis Visit	Value						Change from Baseline					
	n	Mean	SD	Min	Med	Max	n	Mean	SD	Min	Med	Max
EV + Pembro (N=170)												
Baseline	160	21.48	6.65	0.0	23.00	28.0						
Pre-surgery week 4	134	21.06	5.96	0.0	21.50	28.0	132	-0.09	6.52	-24.0	-0.17	28.0
Pre-surgery week 7	130	21.54	5.31	2.3	22.00	28.0	127	-0.37	4.83	-11.8	-1.00	26.8
Pre-surgery week 10	142	20.54	6.44	0.0	21.50	28.0	138	-1.02	6.43	-25.0	-1.00	28.0
Post-surgery week 9	125	20.25	5.98	0.0	21.00	28.0	122	-1.12	6.95	-22.2	-1.58	28.0
Post-surgery week 12	84	20.46	6.41	3.5	21.00	28.0	83	-1.25	6.92	-18.2	-1.17	28.0
Post-surgery week 18	106	20.33	6.29	0.0	21.00	28.0	102	-0.62	6.44	-15.7	-1.00	21.0
Post-surgery week 30	95	20.42	6.30	0.0	21.00	28.0	90	-1.19	6.53	-19.0	-1.00	28.0
Post-surgery week 42	87	19.94	6.21	0.0	21.00	28.0	83	-1.04	7.82	-27.0	-1.17	28.0
Post-surgery week 54	80	20.64	5.92	2.3	21.00	28.0	78	-0.68	6.02	-14.8	-1.00	28.0
Post-surgery week 66	54	20.57	6.11	0.0	21.00	28.0	54	-0.46	6.97	-22.2	-0.50	24.0
Post-surgery week 78	47	18.98	6.53	0.0	20.00	28.0	47	-1.73	8.30	-22.5	-2.00	28.0
Post-surgery week 90	43	20.86	6.53	5.8	21.00	28.0	43	-0.03	7.52	-10.0	-1.00	28.0
Post-surgery week 102	33	20.34	5.78	10.5	20.00	28.0	33	-1.20	6.25	-10.5	-2.33	20.0
RC + PLND (N=174)												
Baseline	128	20.25	6.19	0.0	21.00	28.0						
Post-surgery week 9	102	20.34	5.99	0.0	21.00	28.0	97	-0.62	5.54	-22.2	0.00	16.0
Post-surgery week 18	79	19.60	6.56	0.0	20.00	28.0	75	-0.99	7.26	-27.0	-1.00	17.5
Post-surgery week 30	68	18.37	6.00	0.0	19.00	28.0	66	-1.95	5.99	-17.0	-2.00	16.0
Post-surgery week 42	57	19.89	6.03	0.0	21.00	28.0	54	-0.86	5.77	-17.0	-0.42	10.0
Post-surgery week 54	48	19.74	6.66	0.0	21.00	28.0	45	-1.06	6.82	-21.0	-1.00	18.0
Post-surgery week 66	35	19.83	6.23	0.0	20.00	28.0	33	-1.39	5.15	-15.0	0.00	8.7
Post-surgery week 78	24	20.78	6.45	1.0	21.50	28.0	22	-1.95	6.97	-25.0	-1.17	14.0
Post-surgery week 90	25	19.97	6.29	5.0	21.00	28.0	22	-1.67	3.24	-6.0	-1.67	5.0
Post-surgery week 102	19	22.12	6.35	0.0	23.33	28.0	17	-1.76	7.17	-25.0	-2.00	12.8

Abbreviations: EV=enfortumab vedotin; FACT-BL-Cys=functional assessment of cancer therapy-bladder-cystectomy; Max=maximum; Med=median; Min=minimum; N=number of patients; n=number of patients with non-missing values; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy; SD=standard deviation.
Note: Baseline is the neoadjuvant cycle 1 assessment or the pre-surgery assessment if patients do not take neoadjuvant treatment.
The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.3004.3.1.1: FACT-Bl-Cys - Summary of Linear Mixed Model of Change from Baseline of FACT-Bl-Cys Subscale
ITT2 Analysis Set

	EV + Pembro (N=170)			RC + PLND (N=174)			EV + Pembro vs. RC + PLND		
Visit	N	LS-Means SE]	95% CI for LS-Means	N	LS-Means [SE]	95% CI for LS-Means	Difference of LS-Means [SE]	95% CI for Difference	p-value
Post-surgery week 18	102	0.89 [0.46]	[-0.02 , 1.81]	75	0.99 [0.61]	[-0.21 , 2.20]	-0.10 [0.77]	[-1.62 , 1.41]	0.8941
Overall	157	1.02 [0.49]	[0.06 , 1.99]	104	1.59 [0.64]	[0.32 , 2.85]	-0.56 [0.81]	[-2.16 , 1.03]	0.4867
Hedges' g							-0.09	[-0.34 , 0.16]	
Convergence Status of Linear Mixed Model: Convergence criteria met.									

Abbreviations: CI=confidence interval;EV=enfortumab vedotin; FACT-BL-Cys=functional assessment of cancer therapy-bladder-cystectomy; LS=least squares; MMRM=mixed model repeated measures; N=number of subjects; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy; SE=standard error.
Note: Linear mixed effects model with factors treatment, time (continuous), baseline, treatment*time as cofactors.
The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.3004.3.2.1: FACT-Bl-Cys - Summary of Linear Mixed Model of Change from Baseline of FACT-Bl-Cys Total Score
ITT2 Analysis Set

	EV + Pembro (N=170)			RC + PLND (N=174)			EV + Pembro vs. RC + PLND		
Visit	N	LS-Means SE]	95% CI for LS-Means	N	LS-Means [SE]	95% CI for LS-Means	Difference of LS-Means [SE]	95% CI for Difference	p-value
Post-surgery week 18	102	-3.60 [1.22]	[-6.01 , -1.20]	75	-3.08 [1.59]	[-6.21 , 0.05]	-0.52 [2.01]	[-4.47 , 3.43]	0.7946
Overall	157	-3.16 [1.29]	[-5.70 , -0.62]	104	-1.80 [1.68]	[-5.11 , 1.51]	-1.36 [2.12]	[-5.54 , 2.81]	0.5207
Hedges' g							-0.08	[-0.33 , 0.17]	
Convergence Status of Linear Mixed Model: Convergence criteria met.									

Abbreviations: CI=confidence interval;EV=enfortumab vedotin; FACT-BL-Cys=functional assessment of cancer therapy-bladder-cystectomy; LS=least squares; MMRM=mixed model repeated measures; N=number of subjects; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy; SE=standard error.
Note: Linear mixed effects model with factors treatment, time (continuous), baseline, treatment*time as cofactors.
The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.3004.3.3.1: FACT-Bl-Cys - Summary of Linear Mixed Model of Change from Baseline of FACT-G Total Score
ITT2 Analysis Set

	EV + Pembro (N=170)			RC + PLND (N=174)			EV + Pembro vs. RC + PLND		
Visit	N	LS-Means SE]	95% CI for LS-Means	N	LS-Means [SE]	95% CI for LS-Means	Difference of LS-Means [SE]	95% CI for Difference	p-value
Post-surgery week 18	102	-4.36 [0.87]	[-6.08 , -2.65]	75	-4.18 [1.14]	[-6.42 , -1.94]	-0.18 [1.43]	[-3.00 , 2.64]	0.8991
Overall	157	-4.03 [0.91]	[-5.82 , -2.25]	104	-3.51 [1.18]	[-5.84 , -1.18]	-0.53 [1.49]	[-3.46 , 2.41]	0.7241
Hedges' g							-0.05	[-0.29 , 0.20]	
Convergence Status of Linear Mixed Model: Convergence criteria met.									

Abbreviations: CI=confidence interval;EV=enfortumab vedotin; FACT-BL-Cys=functional assessment of cancer therapy-bladder-cystectomy; FACT-G=functional assessment of cancer therapy - general; LS=least squares; MMRM=mixed model repeated measures; N=number of subjects; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy; SE=standard error.
Note: Linear mixed effects model with factors treatment, time (continuous), baseline, treatment*time as cofactors.
The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.3004.3.4.1: FACT-Bl-Cys - Summary of Linear Mixed Model of Change from Baseline of Emotional-Well-Being
ITT2 Analysis Set

	EV + Pembro (N=170)			RC + PLND (N=174)			EV + Pembro vs. RC + PLND		
Visit	N	LS-Means SE]	95% CI for LS-Means	N	LS-Means [SE]	95% CI for LS-Means	Difference of LS-Means [SE]	95% CI for Difference	p-value
Post-surgery week 18	102	0.27 [0.23]	[-0.18 , 0.72]	75	0.57 [0.30]	[-0.02 , 1.16]	-0.30 [0.38]	[-1.04 , 0.44]	0.4277
Overall	157	0.35 [0.24]	[-0.13 , 0.82]	104	0.64 [0.31]	[0.03 , 1.26]	-0.30 [0.39]	[-1.08 , 0.48]	0.4503
Hedges' g							-0.10	[-0.34 , 0.15]	
Convergence Status of Linear Mixed Model: Convergence criteria met.									

Abbreviations: CI=confidence interval;EV=enfortumab vedotin; FACT-BL-Cys=functional assessment of cancer therapy-bladder-cystectomy; LS=least squares; MMRM=mixed model repeated measures; N=number of subjects; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy; SE=standard error.
Note: Linear mixed effects model with factors treatment, time (continuous), baseline, treatment*time as cofactors.
The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.3004.3.5.1: FACT-Bl-Cys - Summary of Linear Mixed Model of Change from Baseline of Functional-Well-Being
ITT2 Analysis Set

	EV + Pembro (N=170)			RC + PLND (N=174)			EV + Pembro vs. RC + PLND		
Visit	N	LS-Means SE]	95% CI for LS-Means	N	LS-Means [SE]	95% CI for LS-Means	Difference of LS-Means [SE]	95% CI for Difference	p-value
Post-surgery week 18	102	-1.60 [0.30]	[-2.19 , -1.01]	75	-2.12 [0.40]	[-2.92 , -1.33]	0.52 [0.50]	[-0.47 , 1.51]	0.3009
Overall	157	-1.42 [0.31]	[-2.03 , -0.82]	104	-1.70 [0.41]	[-2.51 , -0.88]	0.27 [0.52]	[-0.74 , 1.29]	0.5980
Hedges' g							0.07	[-0.18 , 0.32]	
Convergence Status of Linear Mixed Model: Convergence criteria met.									

Abbreviations: CI=confidence interval;EV=enfortumab vedotin; FACT-BL-Cys=functional assessment of cancer therapy-bladder-cystectomy; LS=least squares; MMRM=mixed model repeated measures; N=number of subjects; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy; SE=standard error.
Note: Linear mixed effects model with factors treatment, time (continuous), baseline, treatment*time as cofactors.
The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.3004.3.6.1: FACT-Bl-Cys - Summary of Linear Mixed Model of Change from Baseline of Physical-Well-Being
ITT2 Analysis Set

	EV + Pembro (N=170)			RC + PLND (N=174)			EV + Pembro vs. RC + PLND		
Visit	N	LS-Means SE]	95% CI for LS-Means	N	LS-Means [SE]	95% CI for LS-Means	Difference of LS-Means [SE]	95% CI for Difference	p-value
Post-surgery week 18	102	-2.27 [0.27]	[-2.80 , -1.74]	75	-1.43 [0.35]	[-2.13 , -0.73]	-0.84 [0.45]	[-1.72 , 0.03]	0.0592
Overall	157	-2.11 [0.28]	[-2.66 , -1.57]	104	-1.25 [0.36]	[-1.96 , -0.53]	-0.87 [0.46]	[-1.77 , 0.03]	0.0581
Hedges' g							-0.24	[-0.49 , 0.01]	
Convergence Status of Linear Mixed Model: Convergence criteria met.									

Abbreviations: CI=confidence interval;EV=enfortumab vedotin; FACT-BL-Cys=functional assessment of cancer therapy-bladder-cystectomy; LS=least squares; MMRM=mixed model repeated measures; N=number of subjects; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy; SE=standard error.
Note: Linear mixed effects model with factors treatment, time (continuous), baseline, treatment*time as cofactors.
The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

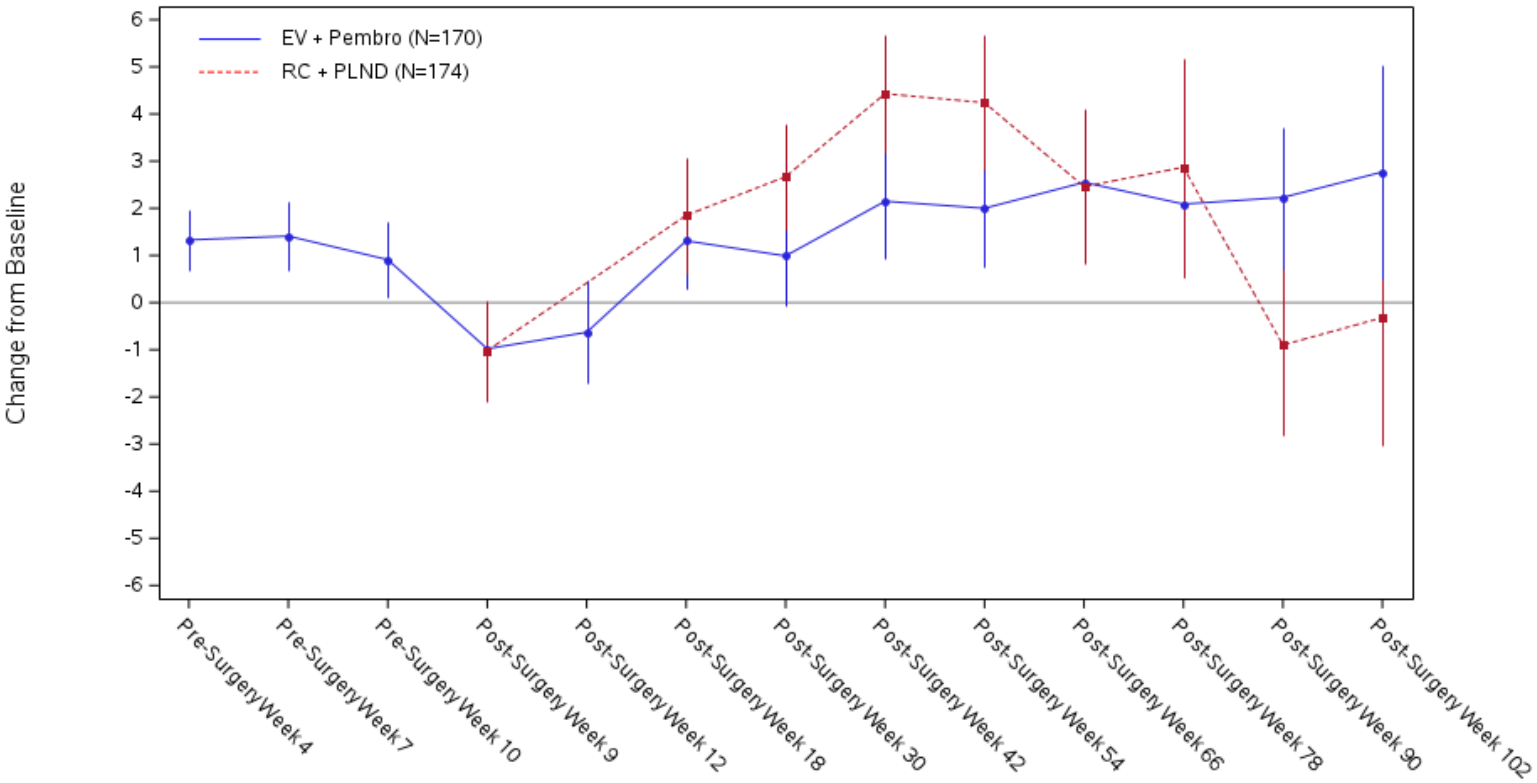
Table 303.1.3004.3.7.1: FACT-Bl-Cys - Summary of Linear Mixed Model of Change from Baseline of Social-Well-Being
ITT2 Analysis Set

	EV + Pembro (N=170)			RC + PLND (N=174)			EV + Pembro vs. RC + PLND		
Visit	N	LS-Means SE]	95% CI for LS-Means	N	LS-Means [SE]	95% CI for LS-Means	Difference of LS-Means [SE]	95% CI for Difference	p-value
Post-surgery week 18	102	-0.64 [0.33]	[-1.28 , 0.01]	75	-1.27 [0.43]	[-2.13 , -0.42]	0.64 [0.54]	[-0.43 , 1.71]	0.2425
Overall	157	-0.71 [0.33]	[-1.37 , -0.05]	104	-1.30 [0.44]	[-2.17 , -0.43]	0.59 [0.55]	[-0.50 , 1.68]	0.2856
Hedges' g							0.14	[-0.11 , 0.39]	
Convergence Status of Linear Mixed Model: Convergence criteria met.									

Abbreviations: CI=confidence interval;EV=enfortumab vedotin; FACT-BL-Cys=functional assessment of cancer therapy-bladder-cystectomy; LS=least squares; MMRM=mixed model repeated measures; N=number of subjects; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy; SE=standard error.
Note: Linear mixed effects model with factors treatment, time (continuous), baseline, treatment*time as cofactors.
The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Endpunkt: FACT-Bl-Cys; Abbildungen

Figure 303.1.3002.3.1.1: FACT-Bl-Cys - Plot of Mean Change from Baseline of FACT-Bl-Cys-Subscale
ITT2 Analysis Set

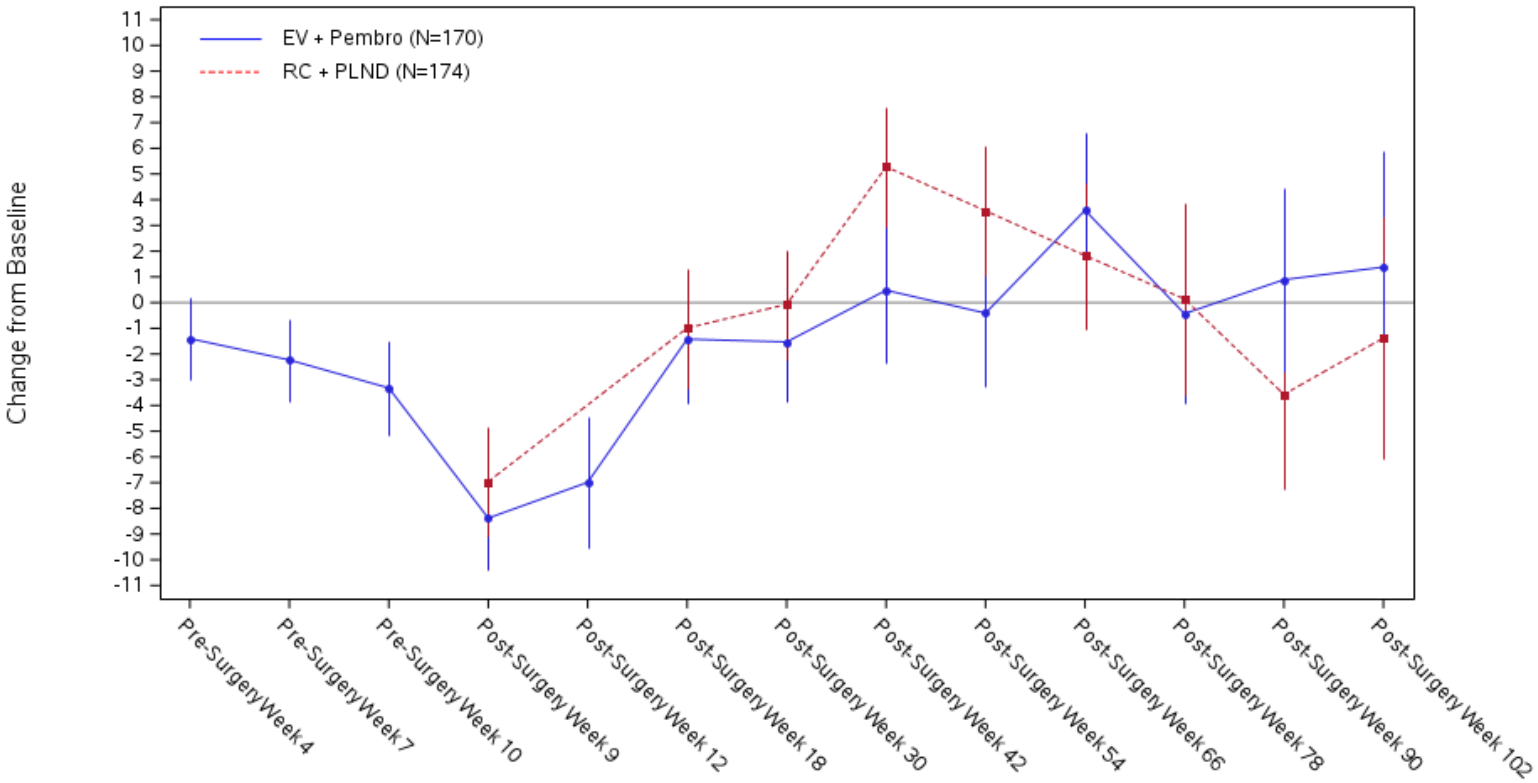


Number of patients

EV + Pembro	132	127	138	122	83	102	90	83	78	54	47	43	33
RC + PLND				97		75	66	54	45	33	22	22	17

Abbreviations: EV=enfortumab vedotin; FACT-BL-Cys=functional assessment of cancer therapy-bladder-cystectomy; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
Note: Baseline is the neoadjuvant cycle 1 assessment or the pre-surgery assessment if patients do not take neoadjuvant treatment.
The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.3002.3.2.1: FACT-Bl-Cys - Plot of Mean Change from Baseline of FACT-BL-Cys Total Score
ITT2 Analysis Set

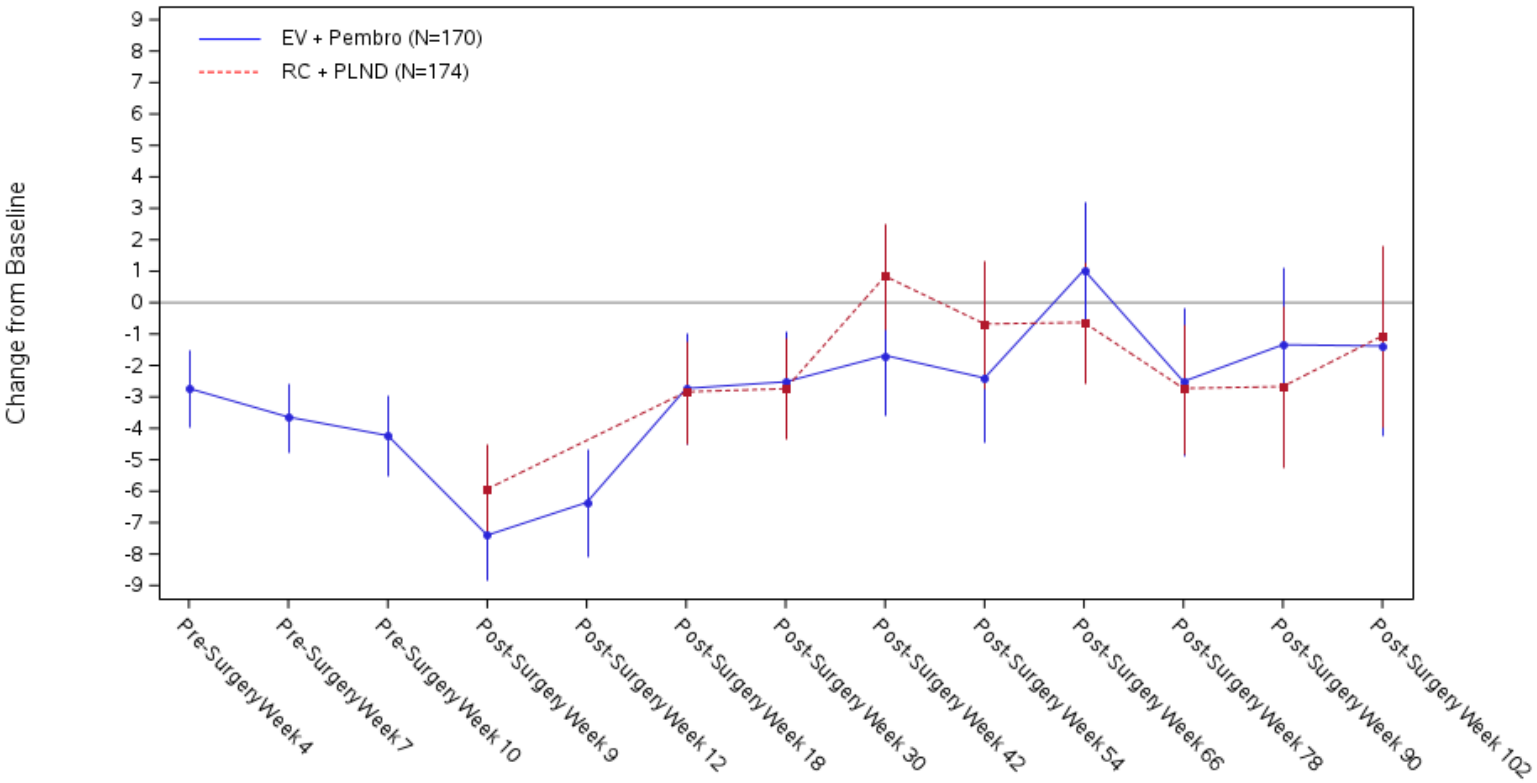


Number of patients

EV + Pembro	132	127	138	122	83	102	90	83	78	54	47	43	33
RC + PLND				97		75	66	54	45	33	22	22	17

Abbreviations: EV=enfortumab vedotin; FACT-BL-Cys=functional assessment of cancer therapy-bladder-cystectomy; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
Note: Baseline is the neoadjuvant cycle 1 assessment or the pre-surgery assessment if patients do not take neoadjuvant treatment.
The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.3002.3.3.1: FACT-Bl-Cys - Plot of Mean Change from Baseline of FACT-G Total Score
ITT2 Analysis Set

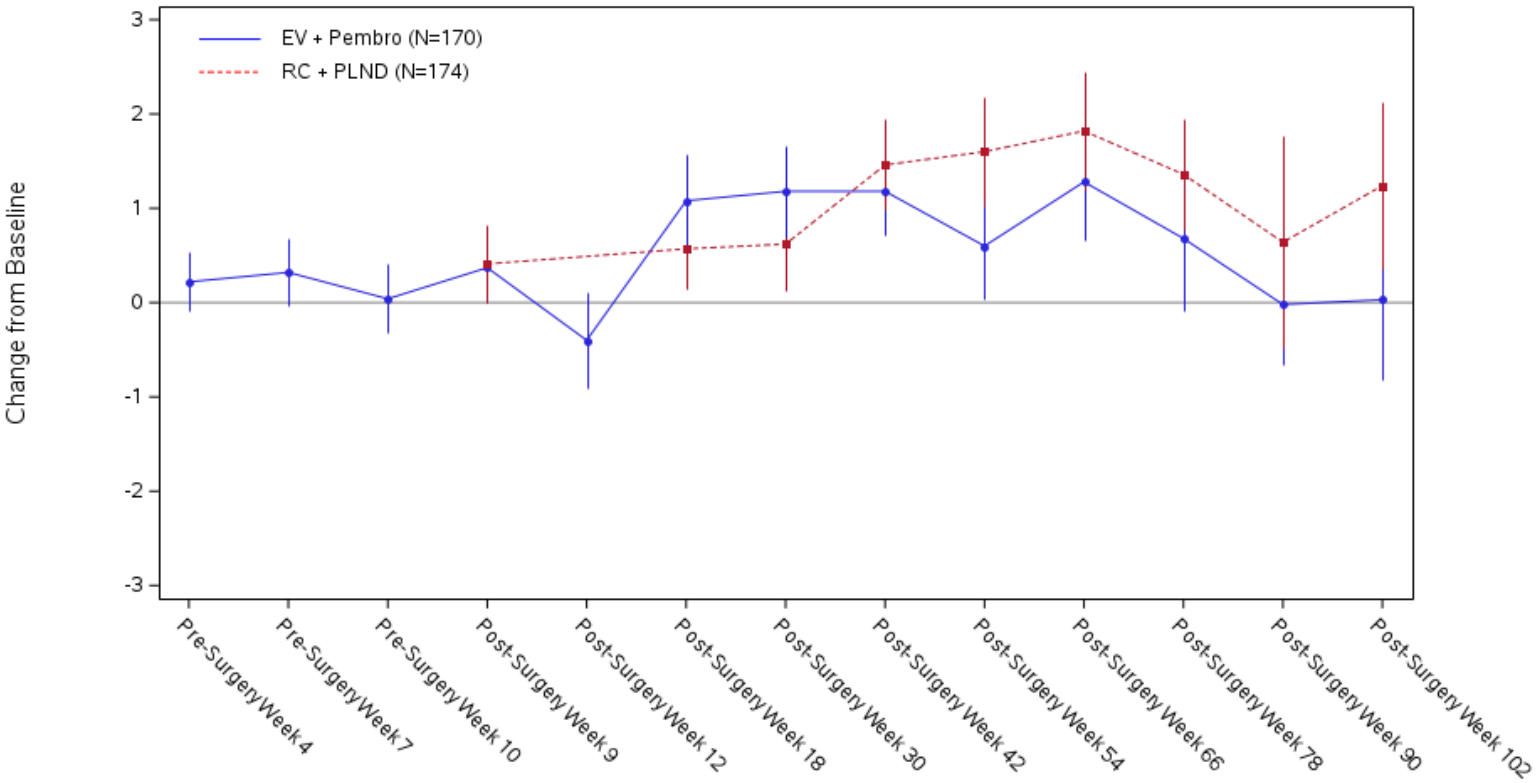


Number of patients

EV + Pembro	132	127	138	122	83	102	90	83	78	54	47	43	33
RC + PLND				97		75	66	54	45	33	22	22	17

Abbreviations: EV=enfortumab vedotin; FACT-BL-Cys=functional assessment of cancer therapy-bladder-cystectomy; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
Note: Baseline is the neoadjuvant cycle 1 assessment or the pre-surgery assessment if patients do not take neoadjuvant treatment.
The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.3002.3.4.1: FACT-Bl-Cys - Plot of Mean Change from Baseline of Emotional Well-Being
ITT2 Analysis Set

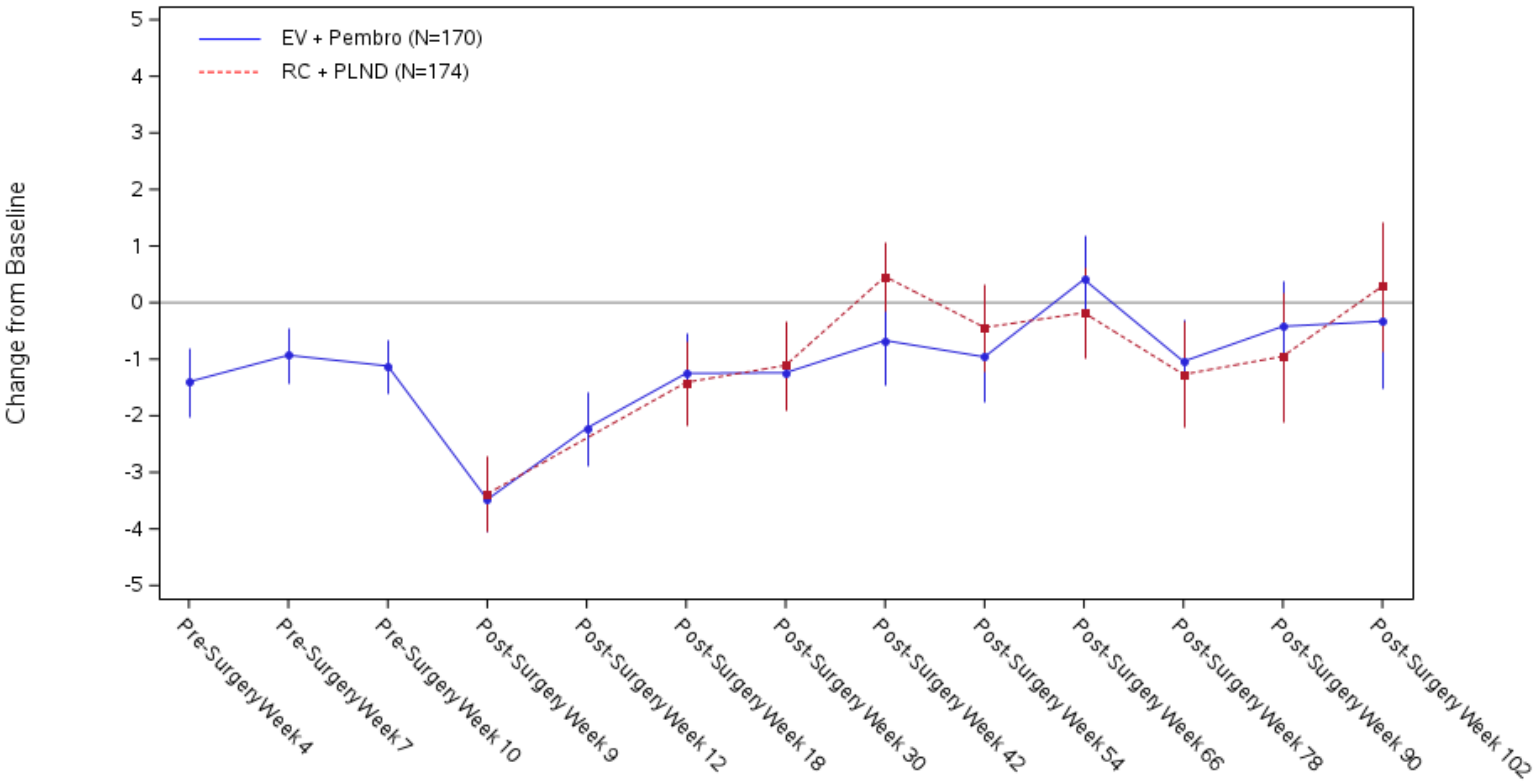


Number of patients

EV + Pembro	132	127	138	122	83	102	90	83	78	54	47	43	33
RC + PLND				97		75	66	54	45	33	22	22	17

Abbreviations: EV=enfortumab vedotin; FACT-BL-Cys=functional assessment of cancer therapy-bladder-cystectomy; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
Note: Baseline is the neoadjuvant cycle 1 assessment or the pre-surgery assessment if patients do not take neoadjuvant treatment.
The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.3002.3.5.1: FACT-Bl-Cys - Plot of Mean Change from Baseline of Functional Well-Being
ITT2 Analysis Set

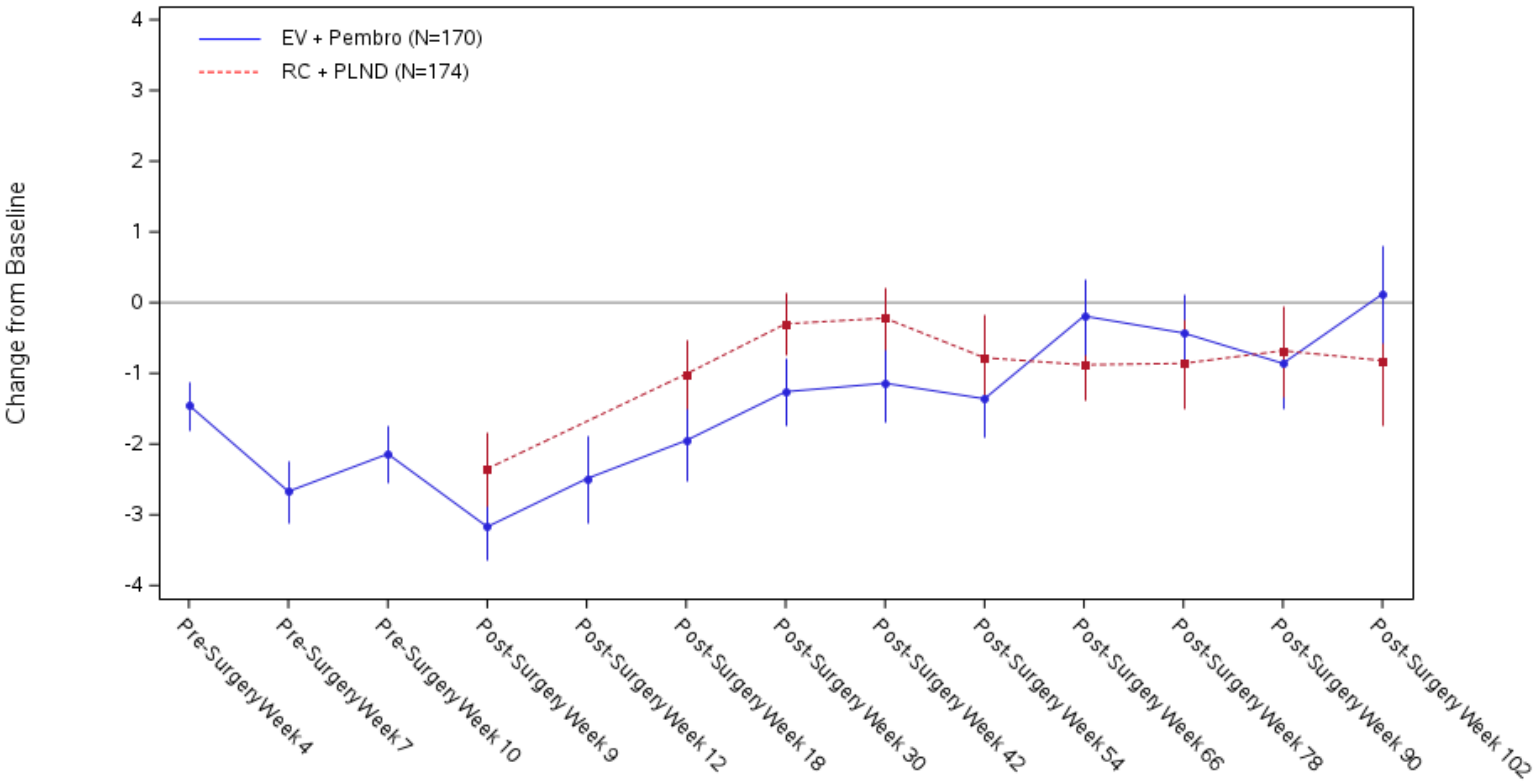


Number of patients

EV + Pembro	132	127	138	122	83	102	90	83	78	54	47	43	33
RC + PLND				97		75	66	54	45	33	22	22	17

Abbreviations: EV=enfortumab vedotin; FACT-BL-Cys=functional assessment of cancer therapy-bladder-cystectomy; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
Note: Baseline is the neoadjuvant cycle 1 assessment or the pre-surgery assessment if patients do not take neoadjuvant treatment.
The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.3002.3.6.1: FACT-Bl-Cys - Plot of Mean Change from Baseline of Physical Well-Being
ITT2 Analysis Set

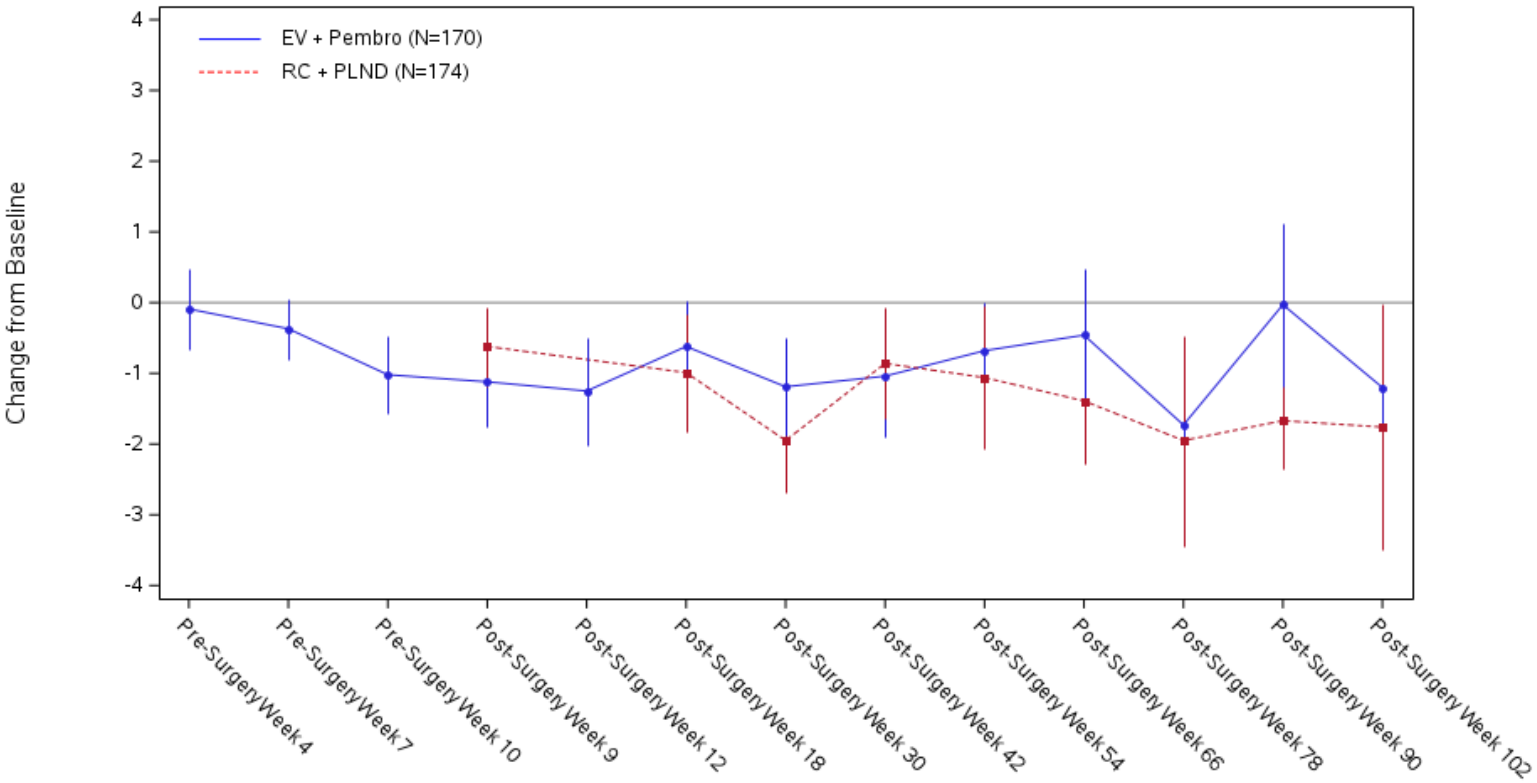


Number of patients

EV + Pembro	132	127	138	122	83	102	90	83	78	54	47	43	33
RC + PLND				97		75	66	54	45	33	22	22	17

Abbreviations: EV=enfortumab vedotin; FACT-BL-Cys=functional assessment of cancer therapy-bladder-cystectomy; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
Note: Baseline is the neoadjuvant cycle 1 assessment or the pre-surgery assessment if patients do not take neoadjuvant treatment.
The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.3002.3.7.1: FACT-Bl-Cys - Plot of Mean Change from Baseline of Social/Family Well-Being
ITT2 Analysis Set



Number of patients

EV + Pembro	132	127	138	122	83	102	90	83	78	54	47	43	33
RC + PLND				97		75	66	54	45	33	22	22	17

Abbreviations: EV=enfortumab vedotin; FACT-BL-Cys=functional assessment of cancer therapy-bladder-cystectomy; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
Note: Baseline is the neoadjuvant cycle 1 assessment or the pre-surgery assessment if patients do not take neoadjuvant treatment.
The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Endpunkt: Bladder Cancer Index (BCI)

Endpunkt: Bladder Cancer Index (BCI); Tabellen

Table 303.1.3000.1: Bladder Cancer Index - Summary of Duration of Observation Time
ITT2 Analysis Set

	EV + Pembro (N=170)	RC + PLND (N=174)
Duration of observation period (months)		
n	165	132
Mean (SD)	14.1 (9.05)	10.1 (8.47)
Median	14.3	9.2
Q1 - Q3	5.6 - 23.7	2.3 - 16.2
Min - Max	0 - 29	0 - 26

Abbreviations: EV=enfortumab vedotin; Max=maxium; Min=minimum; N=number of patients; n=number of patients with non-missing values; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; Q1=first quartile; Q3=third quartile; RC=radical cystectomy; SD=standard deviation.
Note:The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
Observation time for BCI questionnaire is defined as the time from randomisation until last date data were collected for BCI questionnaire.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.3001.1: Bladder Cancer Index - Return Rates
ITT2 Analysis Set

Analysis Visit	EV+Pembro (N=170)			RC+PLND (N=174)		
	Compliance rate	Modified completion rate	Completion rate	Compliance rate	Modified completion rate	Completion rate
Baseline	157 / 169 (92.9%)	157 / 170 (92.4%)	157 / 170 (92.4%)	122 / 138 (88.4%)	122 / 174 (70.1%)	122 / 174 (70.1%)
Pre-surgery week 4	132 / 153 (86.3%)	132 / 170 (77.6%)	132 / 170 (77.6%)	0	0 / 174 (0.0%)	0 / 174 (0.0%)
Pre-surgery week 7	127 / 151 (84.1%)	127 / 169 (75.1%)	127 / 170 (74.7%)	0	0 / 174 (0.0%)	0 / 174 (0.0%)
Pre-surgery week 10	138 / 156 (88.5%)	138 / 168 (82.1%)	138 / 170 (81.2%)	0	0 / 174 (0.0%)	0 / 174 (0.0%)
Post-surgery week 9	123 / 142 (86.6%)	123 / 167 (73.7%)	123 / 170 (72.4%)	97 / 125 (77.6%)	97 / 166 (58.4%)	97 / 174 (55.7%)
Post-surgery week 12	85 / 101 (84.2%)	85 / 163 (52.1%)	85 / 170 (50.0%)	0	0 / 164 (0.0%)	0 / 174 (0.0%)
Post-surgery week 18	107 / 124 (86.3%)	107 / 160 (66.9%)	107 / 170 (62.9%)	73 / 89 (82.0%)	73 / 149 (49.0%)	73 / 174 (42.0%)
Post-surgery week 30	95 / 115 (82.6%)	95 / 150 (63.3%)	95 / 170 (55.9%)	65 / 80 (81.3%)	65 / 141 (46.1%)	65 / 174 (37.4%)
Post-surgery week 42	85 / 104 (81.7%)	85 / 146 (58.2%)	85 / 170 (50.0%)	54 / 72 (75.0%)	54 / 134 (40.3%)	54 / 174 (31.0%)
Post-surgery week 54	80 / 92 (87.0%)	80 / 140 (57.1%)	80 / 170 (47.1%)	47 / 57 (82.5%)	47 / 124 (37.9%)	47 / 174 (27.0%)
Post-surgery week 66	54 / 71 (76.1%)	54 / 140 (38.6%)	54 / 170 (31.8%)	34 / 44 (77.3%)	34 / 122 (27.9%)	34 / 174 (19.5%)
Post-surgery week 78	47 / 59 (79.7%)	47 / 138 (34.1%)	47 / 170 (27.6%)	24 / 30 (80.0%)	24 / 119 (20.2%)	24 / 174 (13.8%)
Post-surgery week 90	43 / 50 (86.0%)	43 / 137 (31.4%)	43 / 170 (25.3%)	22 / 27 (81.5%)	22 / 116 (19.0%)	22 / 174 (12.6%)
Post-surgery week 102	33 / 45 (73.3%)	33 / 136 (24.3%)	33 / 170 (19.4%)	18 / 22 (81.8%)	18 / 116 (15.5%)	18 / 174 (10.3%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
Note: The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
Modified completion rate is defined as the proportion of patients who completed the instrument among the ITT analysis sets while accounting for deaths.
Compliance rate is defined as the proportion of patients who completed the instrument among those who were expected to complete at a given visit
Completion rate is defined as the proportion of patients who completed the instrument among the ITT2 analysis set.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.3002.1.1.1: Bladder Cancer Index - Observed Means and Change from Baseline of Bowel Summary
ITT2 Analysis Set

Treatment Group Analysis Visit	Value						Change from Baseline					
	n	Mean	SD	Min	Med	Max	n	Mean	SD	Min	Med	Max
EV + Pembro (N=170)												
Baseline	157	85.61	14.47	33.3	90.00	100.0						
Pre-surgery week 4	132	81.79	15.75	20.8	85.85	100.0	130	-2.58	14.30	-71.7	-2.50	52.5
Pre-surgery week 7	127	83.38	13.70	38.3	87.50	100.0	123	-2.11	15.14	-54.2	-2.50	52.5
Pre-surgery week 10	138	83.22	14.48	40.0	88.35	100.0	134	-3.18	15.49	-40.9	-2.50	57.5
Post-surgery week 9	123	77.63	17.42	19.2	81.70	100.0	119	-9.07	17.84	-67.5	-7.50	40.8
Post-surgery week 12	85	79.81	16.46	30.8	84.20	100.0	82	-7.97	18.92	-65.9	-6.25	37.5
Post-surgery week 18	107	81.46	16.82	25.0	86.70	100.0	101	-4.75	20.14	-75.0	-2.50	57.5
Post-surgery week 30	95	84.46	13.47	50.8	90.00	100.0	88	-2.32	16.17	-44.2	-2.10	50.0
Post-surgery week 42	85	84.28	13.16	47.5	86.70	100.0	79	-2.05	16.08	-45.0	0.00	52.5
Post-surgery week 54	80	81.44	16.38	27.5	85.00	100.0	77	-5.58	19.18	-70.0	-2.50	44.2
Post-surgery week 66	54	83.18	14.79	35.8	86.25	100.0	53	-2.69	15.22	-52.5	0.00	32.5
Post-surgery week 78	47	82.11	15.63	27.5	82.50	100.0	46	-6.02	17.87	-65.0	-2.50	25.0
Post-surgery week 90	43	84.03	15.46	33.3	87.50	100.0	43	-4.21	18.05	-60.9	0.00	30.0
Post-surgery week 102	33	83.12	14.57	51.7	86.70	100.0	33	-5.45	15.00	-42.5	-2.50	18.3
RC + PLND (N=174)												
Baseline	122	83.49	15.12	43.3	87.50	100.0						
Post-surgery week 9	97	74.77	15.92	35.0	76.70	100.0	92	-9.49	19.24	-47.5	-7.90	47.5
Post-surgery week 18	73	81.11	12.94	47.5	82.50	100.0	70	-4.27	15.35	-47.5	-5.00	40.0
Post-surgery week 30	65	83.16	12.43	50.0	85.00	100.0	63	-3.20	15.95	-45.0	-5.00	41.7
Post-surgery week 42	54	82.46	14.19	47.5	84.60	100.0	52	-2.59	13.57	-47.5	-2.50	28.3
Post-surgery week 54	47	83.78	14.53	48.3	87.50	100.0	43	-4.57	14.76	-48.3	-2.50	20.0
Post-surgery week 66	34	83.14	12.36	46.7	85.00	100.0	32	-4.58	15.88	-53.3	-1.65	21.7
Post-surgery week 78	24	81.67	14.95	38.3	85.00	100.0	21	-6.39	11.50	-41.7	-5.00	12.5
Post-surgery week 90	22	82.47	16.08	45.8	85.00	100.0	19	-6.05	19.78	-42.5	-1.70	24.2
Post-surgery week 102	18	79.59	18.78	39.2	85.45	100.0	15	-9.78	18.86	-51.7	-5.00	20.0

Abbreviations: EV=enfortumab vedotin; Max=maximum; Med=median; Min=minimum; N=number of patients; n=number of patients with non-missing values; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy; SD=standard deviation.
Note: Baseline is the neoadjuvant cycle 1 assessment or the pre-surgery assessment if patients do not take neoadjuvant treatment.
The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.3002.1.2.1: Bladder Cancer Index - Observed Means and Change from Baseline of Sexual Summary
ITT2 Analysis Set

Treatment Group Analysis Visit	Value						Change from Baseline					
	n	Mean	SD	Min	Med	Max	n	Mean	SD	Min	Med	Max
EV + Pembro (N=170)												
Baseline	152	49.74	24.93	8.3	49.67	100.0						
Pre-surgery week 4	125	48.71	23.13	8.3	44.42	100.0	123	0.34	17.41	-48.6	0.00	45.8
Pre-surgery week 7	119	46.91	25.21	8.3	41.67	100.0	114	-2.02	17.98	-50.0	0.00	59.0
Pre-surgery week 10	130	45.54	25.04	6.3	41.67	100.0	126	-4.08	22.00	-56.9	0.00	70.8
Post-surgery week 9	116	31.22	19.59	0.0	30.54	100.0	111	-18.56	24.37	-88.9	-14.58	45.8
Post-surgery week 12	81	33.69	19.19	8.3	37.50	91.7	77	-16.68	27.33	-70.8	-14.58	45.8
Post-surgery week 18	102	35.07	22.20	6.3	35.08	100.0	94	-15.46	24.77	-64.6	-10.42	47.9
Post-surgery week 30	90	36.39	22.74	8.3	35.42	100.0	82	-13.32	24.94	-68.8	-9.38	60.2
Post-surgery week 42	82	35.72	20.15	8.3	39.58	100.0	75	-12.10	25.29	-60.4	-10.42	57.5
Post-surgery week 54	77	36.81	21.28	8.3	41.67	97.3	74	-11.64	24.29	-64.6	-8.33	43.1
Post-surgery week 66	50	35.31	22.73	4.2	37.97	100.0	48	-8.46	23.59	-64.6	-5.54	45.8
Post-surgery week 78	44	37.55	21.74	8.3	40.63	89.6	42	-8.57	25.75	-66.7	-4.17	35.4
Post-surgery week 90	39	34.88	23.93	8.3	33.33	92.3	38	-11.53	25.76	-72.3	-10.42	50.7
Post-surgery week 102	30	33.03	23.48	4.2	36.08	83.3	30	-14.26	28.45	-72.9	-14.58	33.3
RC + PLND (N=174)												
Baseline	119	43.65	22.38	6.3	41.67	100.0						
Post-surgery week 9	93	31.54	18.63	6.3	33.33	91.7	87	-15.38	24.00	-74.6	-10.42	33.3
Post-surgery week 18	65	31.00	17.69	8.3	27.75	79.2	61	-17.88	25.30	-81.3	-16.67	41.7
Post-surgery week 30	61	33.17	17.43	2.1	33.33	66.7	58	-15.50	25.31	-78.5	-11.46	31.3
Post-surgery week 42	52	37.83	20.18	8.3	40.63	90.3	49	-11.18	24.27	-67.3	-8.33	42.3
Post-surgery week 54	46	33.59	20.85	8.3	37.17	75.0	41	-18.00	26.82	-72.9	-11.83	36.1
Post-surgery week 66	33	35.30	22.64	8.3	33.33	83.3	31	-17.62	24.48	-72.3	-10.42	20.8
Post-surgery week 78	21	28.28	18.29	8.3	22.92	72.9	19	-15.78	18.89	-62.5	-13.92	18.8
Post-surgery week 90	21	28.63	20.44	8.3	22.92	84.8	18	-22.30	23.85	-62.5	-12.17	6.3
Post-surgery week 102	17	29.32	19.87	8.3	25.00	66.7	14	-24.21	21.44	-62.5	-21.50	0.0

Abbreviations: EV=enfortumab vedotin; Max=maximum; Med=median; Min=minimum; N=number of patients; n=number of patients with non-missing values; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy; SD=standard deviation.
Note: Baseline is the neoadjuvant cycle 1 assessment or the pre-surgery assessment if patients do not take neoadjuvant treatment.
The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.3002.1.3.1: Bladder Cancer Index - Observed Means and Change from Baseline of Urinary Summary
ITT2 Analysis Set

Treatment Group Analysis Visit	Value						Change from Baseline					
	n	Mean	SD	Min	Med	Max	n	Mean	SD	Min	Med	Max
EV + Pembro (N=170)												
Baseline	157	83.11	16.65	29.2	87.50	100.0						
Pre-surgery week 4	132	83.70	15.54	27.0	85.79	100.0	130	2.04	12.92	-32.1	1.38	38.8
Pre-surgery week 7	127	85.55	16.29	31.9	91.67	100.0	123	2.60	14.45	-34.8	2.08	45.1
Pre-surgery week 10	138	86.14	16.24	27.1	91.67	100.0	134	2.63	15.38	-50.0	1.04	44.5
Post-surgery week 9	123	75.37	20.08	18.8	79.17	100.0	119	-7.03	22.77	-81.3	-4.83	49.3
Post-surgery week 12	85	78.56	17.06	24.3	83.33	100.0	82	-5.82	22.67	-75.8	-4.17	54.9
Post-surgery week 18	107	80.09	17.66	25.6	85.42	100.0	101	-2.03	20.74	-57.0	-3.42	60.4
Post-surgery week 30	95	80.72	17.05	24.9	84.75	100.0	88	-1.64	18.91	-47.9	-0.04	52.1
Post-surgery week 42	85	80.47	18.17	8.3	85.42	100.0	79	-1.10	22.12	-86.2	-0.08	56.3
Post-surgery week 54	80	82.18	16.60	29.2	85.42	100.0	77	0.19	19.50	-57.0	0.00	50.8
Post-surgery week 66	54	80.93	16.77	43.8	85.42	100.0	53	1.06	21.75	-36.9	0.75	62.5
Post-surgery week 78	47	78.80	16.93	38.2	79.92	100.0	46	-4.15	17.14	-43.1	-3.13	34.0
Post-surgery week 90	43	78.28	19.65	20.8	86.17	100.0	43	-4.45	20.10	-60.4	-0.67	31.9
Post-surgery week 102	33	81.28	16.35	50.7	86.08	100.0	33	-1.48	18.39	-49.3	4.17	34.0
RC + PLND (N=174)												
Baseline	122	74.54	21.78	22.2	77.08	100.0						
Post-surgery week 9	97	73.17	19.24	21.6	77.08	100.0	92	-4.12	27.38	-65.3	-5.21	65.3
Post-surgery week 18	73	76.86	17.08	27.1	77.08	100.0	70	-0.05	24.53	-45.8	0.00	70.8
Post-surgery week 30	65	80.87	13.87	44.4	83.42	100.0	63	2.31	22.27	-52.1	-0.58	70.8
Post-surgery week 42	54	81.11	13.33	43.8	79.92	100.0	52	3.22	23.77	-56.3	-0.71	70.8
Post-surgery week 54	47	83.44	14.84	41.7	89.58	100.0	43	4.82	25.26	-41.7	0.00	70.8
Post-surgery week 66	34	78.67	16.63	35.4	82.29	100.0	32	2.82	24.30	-43.8	0.00	60.4
Post-surgery week 78	24	74.57	19.58	32.6	77.50	100.0	21	0.39	34.63	-41.1	-4.17	70.8
Post-surgery week 90	22	75.20	19.65	36.8	76.79	100.0	19	-0.71	29.53	-46.6	0.00	70.8
Post-surgery week 102	18	76.14	14.94	50.0	76.42	100.0	15	-2.22	33.96	-47.9	-5.50	70.8

Abbreviations: EV=enfortumab vedotin; Max=maximum; Med=median; Min=minimum; N=number of patients; n=number of patients with non-missing values; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy; SD=standard deviation.
Note: Baseline is the neoadjuvant cycle 1 assessment or the pre-surgery assessment if patients do not take neoadjuvant treatment.
The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.3004.1.1.1: Bladder Cancer Index - Summary of Linear Mixed Model of Change from Baseline of Bowel Summary
ITT2 Analysis Set

	EV + Pembro (N=170)			RC + PLND (N=174)			EV + Pembro vs. RC + PLND		
Visit	N	LS-Means SE]	95% CI for LS-Means	N	LS-Means [SE]	95% CI for LS-Means	Difference of LS-Means [SE]	95% CI for Difference	p-value
Post-surgery week 18	101	-4.57 [0.81]	[-6.16 , -2.98]	70	-6.56 [1.09]	[-8.71 , -4.40]	1.98 [1.36]	[-0.69 , 4.66]	0.1454
Overall	154	-4.40 [0.84]	[-6.05 , -2.74]	100	-5.68 [1.14]	[-7.92 , -3.44]	1.28 [1.41]	[-1.50 , 4.07]	0.3654
Hedges' g							0.12	[-0.13 , 0.37]	
Convergence Status of Linear Mixed Model: Convergence criteria met.									

Abbreviations: CI=confidence interval;EV=enfortumab vedotin; LS=least squares; MMRM=mixed model repeated measures; N=number of subjects; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy; SE=standard error.
Note: Linear mixed effects model with factors treatment, time (continuous), baseline, treatment*time as cofactors.
The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.3004.1.2.1: Bladder Cancer Index - Summary of Linear Mixed Model of Change from Baseline of Sexual Summary
ITT2 Analysis Set

	EV + Pembro (N=170)			RC + PLND (N=174)			EV + Pembro vs. RC + PLND		
Visit	N	LS-Means SE]	95% CI for LS-Means	N	LS-Means [SE]	95% CI for LS-Means	Difference of LS-Means [SE]	95% CI for Difference	p-value
Post-surgery week 18	94	-9.10 [1.16]	[-11.39 , -6.81]	61	-15.11 [1.57]	[-18.20 ,-12.02]	6.01 [1.95]	[2.16 , 9.85]	0.0023
Overall	149	-10.42 [1.23]	[-12.85 , -7.98]	94	-14.59 [1.67]	[-17.87 ,-11.31]	4.18 [2.07]	[0.09 , 8.26]	0.0451
Hedges' g							0.27	[0.01 , 0.53]	
Convergence Status of Linear Mixed Model: Convergence criteria met.									

Abbreviations: CI=confidence interval;EV=enfortumab vedotin; LS=least squares; MMRM=mixed model repeated measures; N=number of subjects; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy; SE=standard error.
Note: Linear mixed effects model with factors treatment, time (continuous), baseline, treatment*time as cofactors.
The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

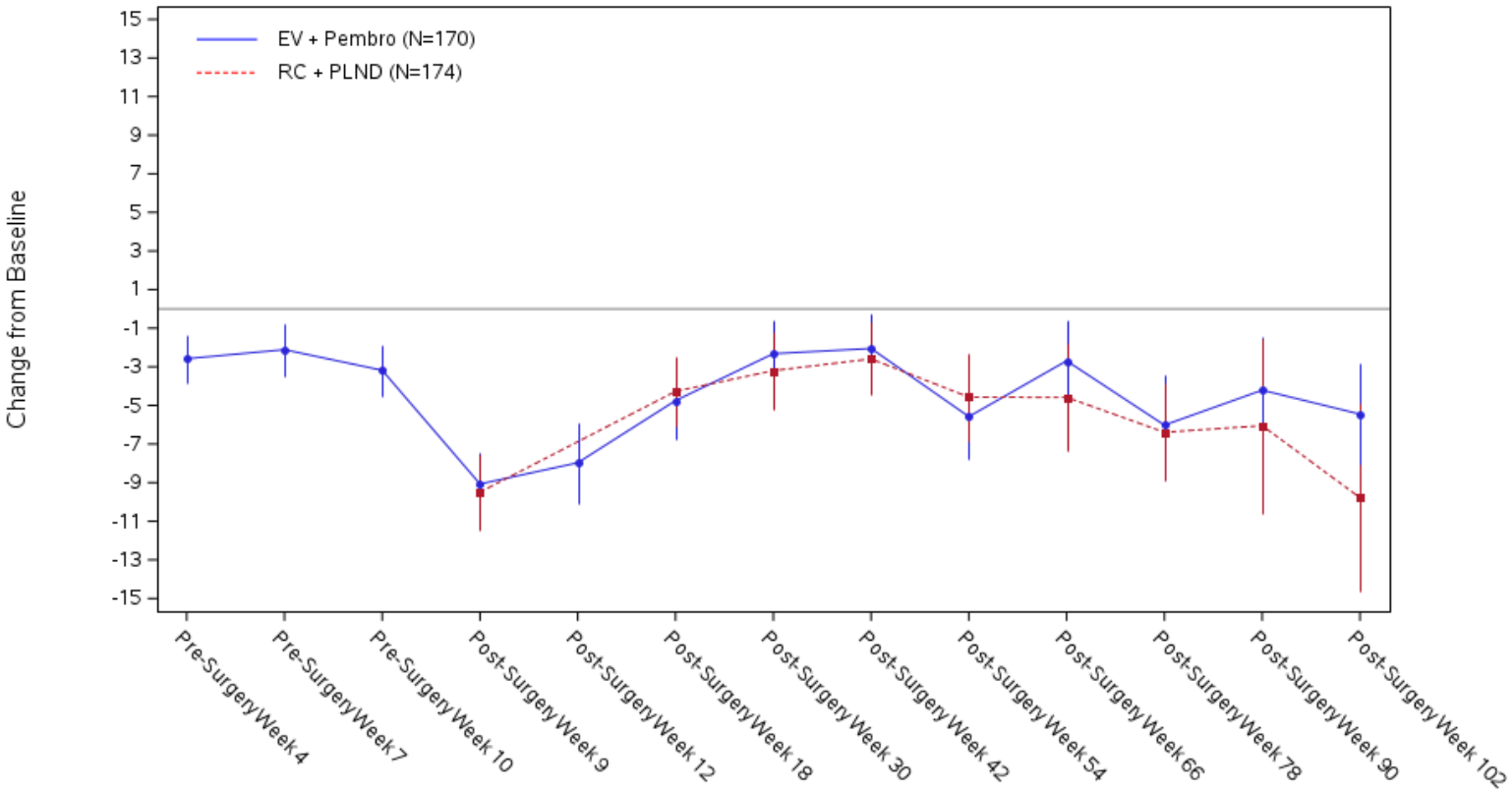
Table 303.1.3004.1.3.1: Bladder Cancer Index - Summary of Linear Mixed Model of Change from Baseline of Urinary Summary
ITT2 Analysis Set

	EV + Pembro (N=170)			RC + PLND (N=174)			EV + Pembro vs. RC + PLND		
Visit	N	LS-Means SE]	95% CI for LS-Means	N	LS-Means [SE]	95% CI for LS-Means	Difference of LS-Means [SE]	95% CI for Difference	p-value
Post-surgery week 18	101	0.45 [0.91]	[-1.35 , 2.24]	70	-2.88 [1.25]	[-5.33 , -0.43]	3.33 [1.55]	[0.27 , 6.38]	0.0330
Overall	154	0.02 [0.98]	[-1.92 , 1.96]	100	-1.91 [1.34]	[-4.56 , 0.73]	1.93 [1.67]	[-1.36 , 5.23]	0.2493
Hedges' g							0.15	[-0.10 , 0.40]	
Convergence Status of Linear Mixed Model: Convergence criteria met.									

Abbreviations: CI=confidence interval;EV=enfortumab vedotin; LS=least squares; MMRM=mixed model repeated measures; N=number of subjects; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy; SE=standard error.
Note: Linear mixed effects model with factors treatment, time (continuous), baseline, treatment*time as cofactors.
The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Endpunkt: Bladder Cancer Index (BCI); Abbildungen

Figure 303.1.3002.1.1.1: Bladder Cancer Index - Plot of Mean Change from Baseline of Bowel Summary
ITT2 Analysis Set

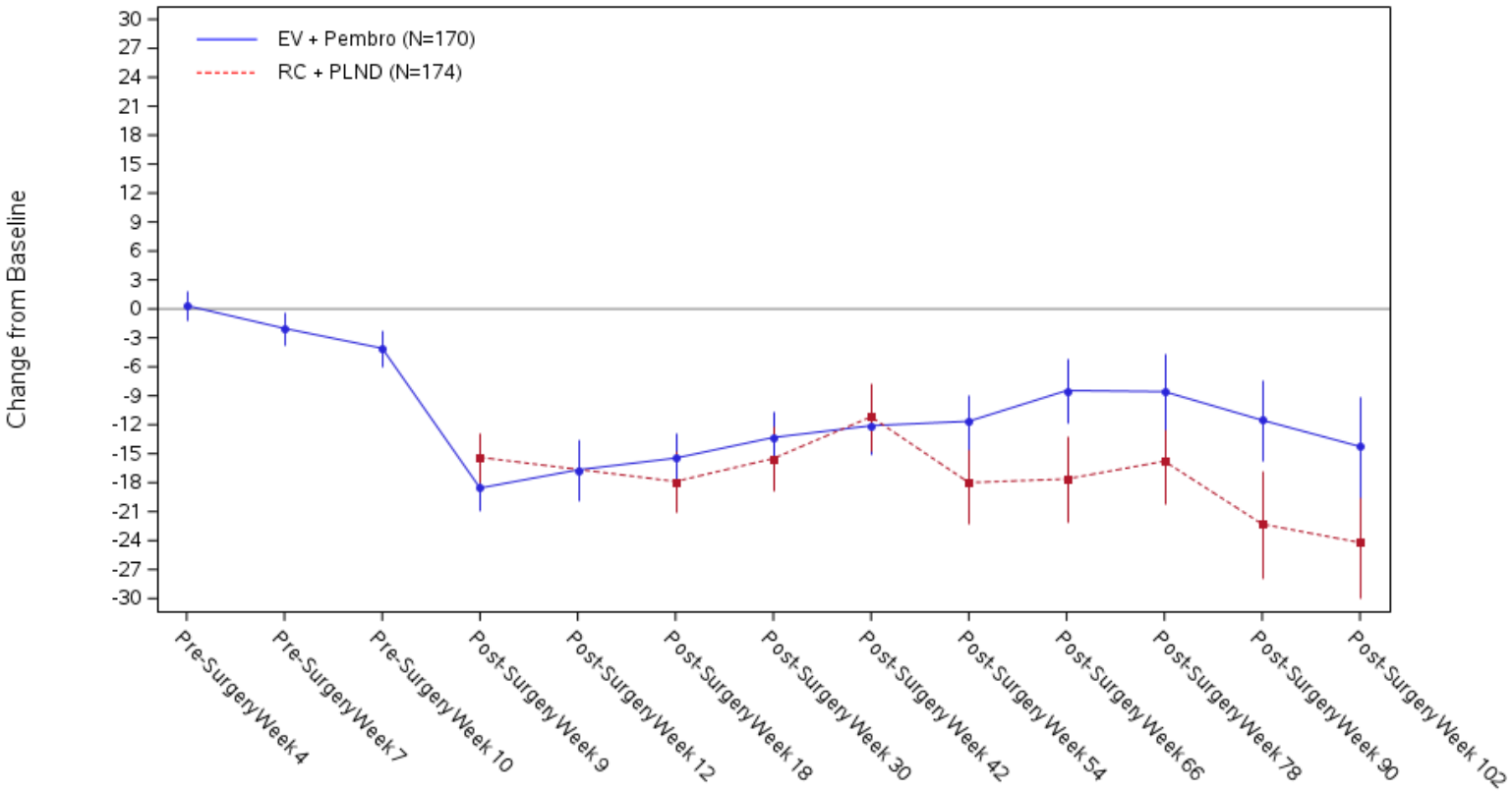


Number of patients

EV + Pembro	130	123	134	119	82	101	88	79	77	53	46	43	33
RC + PLND				92		70	63	52	43	32	21	19	15

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
Note: Baseline is the neoadjuvant cycle 1 assessment or the pre-surgery assessment if patients do not take neoadjuvant treatment.
The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.3002.1.2.1: Bladder Cancer Index - Plot of Mean Change from Baseline of Sexual Summary
ITT2 Analysis Set

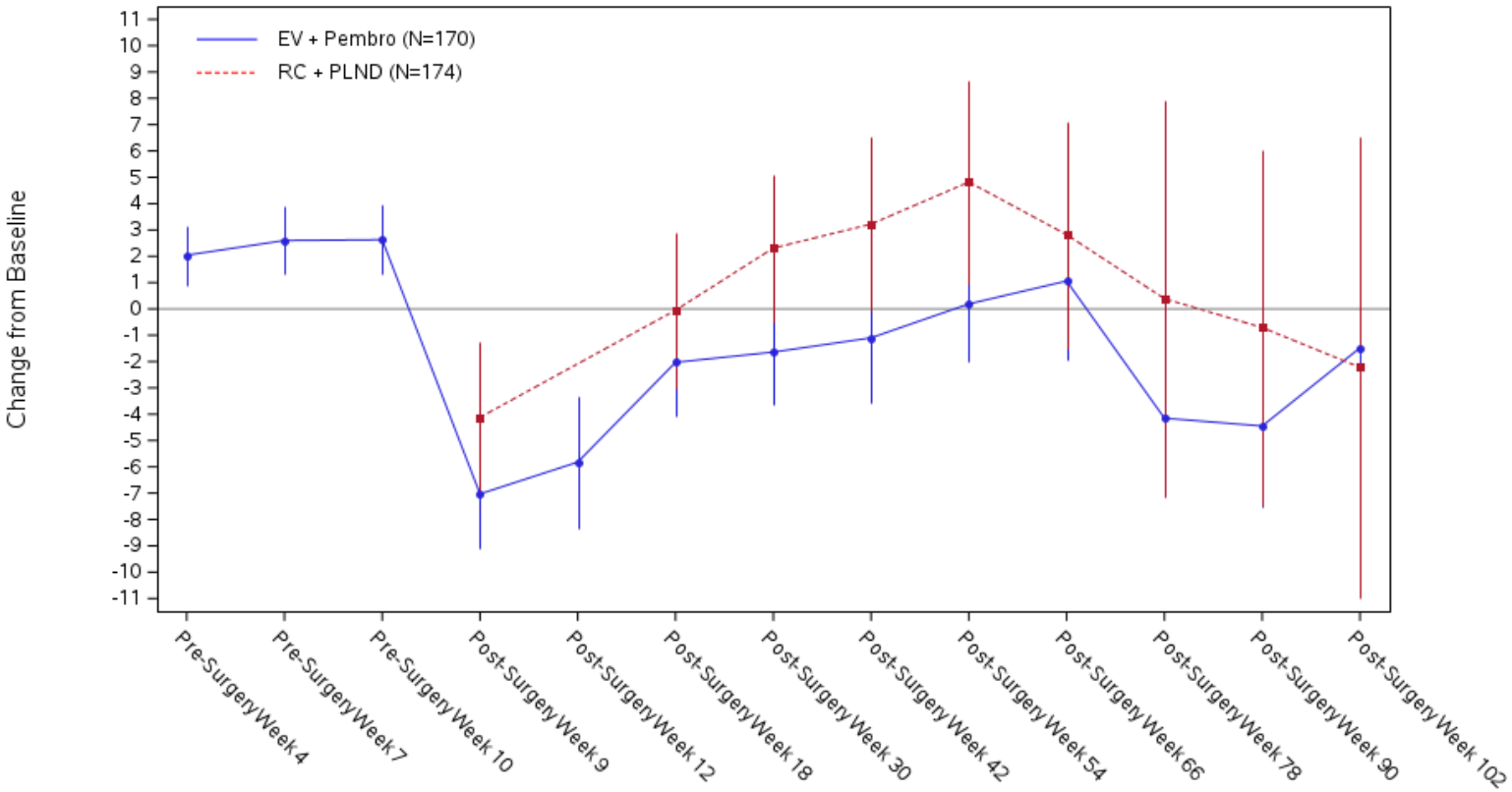


Number of patients

EV + Pembro	123	114	126	111	77	94	82	75	74	48	42	38	30
RC + PLND				87		61	58	49	41	31	19	18	14

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
Note: Baseline is the neoadjuvant cycle 1 assessment or the pre-surgery assessment if patients do not take neoadjuvant treatment.
The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.3002.1.3.1: Bladder Cancer Index - Plot of Mean Change from Baseline of Urinary Summary
ITT2 Analysis Set



Number of patients

EV + Pembro	130	123	134	119	82	101	88	79	77	53	46	43	33
RC + PLND				92		70	63	52	43	32	21	19	15

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
Note: Baseline is the neoadjuvant cycle 1 assessment or the pre-surgery assessment if patients do not take neoadjuvant treatment.
The ITT2 analysis set includes all patients that are randomized into arms B and C in stage 2.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Endpunkt: Unerwünschte Ereignisse

Endpunkt: Unerwünschte Ereignisse; Deskriptive Ergebnisse

Table 303.1.2000.1.1: Frequency Summary of Treatment Emergent Adverse Events in Combined Treatment Phases
SAF2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=167)	RC + PLND (N=159)	Total (N=326)
Overall	167 (100.0%)	103 (64.8%)	270 (82.8%)
Gastrointestinal Disorders	118 (70.7%)	45 (28.3%)	163 (50.0%)
Diarrhoea	57 (34.1%)	5 (3.1%)	62 (19.0%)
Constipation	46 (27.5%)	13 (8.2%)	59 (18.1%)
Nausea	43 (25.7%)	12 (7.5%)	55 (16.9%)
Abdominal Pain	17 (10.2%)	9 (5.7%)	26 (8.0%)
Vomiting	15 (9.0%)	6 (3.8%)	21 (6.4%)
Dry Mouth	18 (10.8%)	1 (0.6%)	19 (5.8%)
Skin And Subcutaneous Tissue Disorders	143 (85.6%)	4 (2.5%)	147 (45.1%)
Pruritus	79 (47.3%)	0	79 (24.2%)
Alopecia	58 (34.7%)	0	58 (17.8%)
Rash	42 (25.1%)	1 (0.6%)	43 (13.2%)
Rash Maculo-Papular	27 (16.2%)	0	27 (8.3%)
Dry Skin	25 (15.0%)	1 (0.6%)	26 (8.0%)
Infections And Infestations	97 (58.1%)	48 (30.2%)	145 (44.5%)
Urinary Tract Infection	40 (24.0%)	20 (12.6%)	60 (18.4%)
General Disorders And Administration Site Conditions	107 (64.1%)	22 (13.8%)	129 (39.6%)
Fatigue	54 (32.3%)	7 (4.4%)	61 (18.7%)
Asthenia	29 (17.4%)	3 (1.9%)	32 (9.8%)
Pyrexia	19 (11.4%)	4 (2.5%)	23 (7.1%)
Oedema Peripheral	16 (9.6%)	3 (1.9%)	19 (5.8%)
Metabolism And Nutrition Disorders	90 (53.9%)	19 (11.9%)	109 (33.4%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are sorted by the descending number of patients in total group. In case of ties, alphabetical order is applied.
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2000.1.1: Frequency Summary of Treatment Emergent Adverse Events in Combined Treatment Phases
SAF2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=167)	RC + PLND (N=159)	Total (N=326)
Decreased Appetite	47 (28.1%)	3 (1.9%)	50 (15.3%)
Hyperglycaemia	21 (12.6%)	1 (0.6%)	22 (6.7%)
Hypokalaemia	16 (9.6%)	4 (2.5%)	20 (6.1%)
Hyperkalaemia	10 (6.0%)	2 (1.3%)	12 (3.7%)
Hyponatraemia	12 (7.2%)	0	12 (3.7%)
Nervous System Disorders	98 (58.7%)	4 (2.5%)	102 (31.3%)
Dysgeusia	47 (28.1%)	0	47 (14.4%)
Peripheral Sensory Neuropathy	23 (13.8%)	0	23 (7.1%)
Neuropathy Peripheral	17 (10.2%)	0	17 (5.2%)
Dizziness	12 (7.2%)	0	12 (3.7%)
Paraesthesia	11 (6.6%)	0	11 (3.4%)
Taste Disorder	11 (6.6%)	0	11 (3.4%)
Investigations	86 (51.5%)	15 (9.4%)	101 (31.0%)
Aspartate Aminotransferase Increased	40 (24.0%)	0	40 (12.3%)
Weight Decreased	33 (19.8%)	5 (3.1%)	38 (11.7%)
Alanine Aminotransferase Increased	32 (19.2%)	2 (1.3%)	34 (10.4%)
Blood Creatinine Increased	19 (11.4%)	6 (3.8%)	25 (7.7%)
Blood And Lymphatic System Disorders	69 (41.3%)	19 (11.9%)	88 (27.0%)
Anaemia	51 (30.5%)	19 (11.9%)	70 (21.5%)
Neutropenia	16 (9.6%)	0	16 (4.9%)
Injury, Poisoning And Procedural Complications	44 (26.3%)	29 (18.2%)	73 (22.4%)
Procedural Pain	9 (5.4%)	12 (7.5%)	21 (6.4%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are sorted by the descending number of patients in total group. In case of ties, alphabetical order is applied.
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2000.1.1: Frequency Summary of Treatment Emergent Adverse Events in Combined Treatment Phases
SAF2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=167)	RC + PLND (N=159)	Total (N=326)
Renal And Urinary Disorders	44 (26.3%)	14 (8.8%)	58 (17.8%)
Acute Kidney Injury	11 (6.6%)	4 (2.5%)	15 (4.6%)
Haematuria	11 (6.6%)	1 (0.6%)	12 (3.7%)
Respiratory, Thoracic And Mediastinal Disorders	45 (26.9%)	12 (7.5%)	57 (17.5%)
Musculoskeletal And Connective Tissue Disorders	39 (23.4%)	4 (2.5%)	43 (13.2%)
Arthralgia	10 (6.0%)	1 (0.6%)	11 (3.4%)
Eye Disorders	41 (24.6%)	0	41 (12.6%)
Lacrimation Increased	16 (9.6%)	0	16 (4.9%)
Dry Eye	10 (6.0%)	0	10 (3.1%)
Vascular Disorders	27 (16.2%)	12 (7.5%)	39 (12.0%)
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)	23 (13.8%)	15 (9.4%)	38 (11.7%)
Prostate Cancer	19 (11.4%)	15 (9.4%)	34 (10.4%)
Psychiatric Disorders	28 (16.8%)	10 (6.3%)	38 (11.7%)
Insomnia	18 (10.8%)	7 (4.4%)	25 (7.7%)
Endocrine Disorders	33 (19.8%)	0	33 (10.1%)
Hypothyroidism	24 (14.4%)	0	24 (7.4%)
Cardiac Disorders	17 (10.2%)	6 (3.8%)	23 (7.1%)
Reproductive System And Breast Disorders	17 (10.2%)	4 (2.5%)	21 (6.4%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are sorted by the descending number of patients in total group. In case of ties, alphabetical order is applied.
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2000.1.1: Frequency Summary of Treatment Emergent Adverse Events in Combined Treatment Phases
SAF2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=167)	RC + PLND (N=159)	Total (N=326)
Hepatobiliary Disorders	16 (9.6%)	1 (0.6%)	17 (5.2%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are sorted by the descending number of patients in total group. In case of ties, alphabetical order is applied.
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2000.1.2.1: Frequency Summary of Treatment Emergent Adverse Events in Preoperative Phase
SAF2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=167)	RC + PLND (N=159)	Total (N=326)
Overall	163 (97.6%)	0	163 (50.0%)
Skin And Subcutaneous Tissue Disorders	132 (79.0%)	0	132 (40.5%)
Pruritus	59 (35.3%)	0	59 (18.1%)
Alopecia	54 (32.3%)	0	54 (16.6%)
Rash	36 (21.6%)	0	36 (11.0%)
Rash Maculo-Papular	22 (13.2%)	0	22 (6.7%)
Dry Skin	17 (10.2%)	0	17 (5.2%)
Gastrointestinal Disorders	82 (49.1%)	0	82 (25.2%)
Diarrhoea	39 (23.4%)	0	39 (12.0%)
Nausea	30 (18.0%)	0	30 (9.2%)
Constipation	24 (14.4%)	0	24 (7.4%)
General Disorders And Administration Site Conditions	75 (44.9%)	0	75 (23.0%)
Fatigue	44 (26.3%)	0	44 (13.5%)
Asthenia	16 (9.6%)	0	16 (4.9%)
Nervous System Disorders	74 (44.3%)	0	74 (22.7%)
Dysgeusia	40 (24.0%)	0	40 (12.3%)
Peripheral Sensory Neuropathy	15 (9.0%)	0	15 (4.6%)
Investigations	59 (35.3%)	0	59 (18.1%)
Aspartate Aminotransferase Increased	35 (21.0%)	0	35 (10.7%)
Alanine Aminotransferase Increased	28 (16.8%)	0	28 (8.6%)
Blood Creatinine Increased	10 (6.0%)	0	10 (3.1%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are sorted by the descending number of patients in total group. In case of ties, alphabetical order is applied.
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2000.1.2.1: Frequency Summary of Treatment Emergent Adverse Events in Preoperative Phase
SAF2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=167)	RC + PLND (N=159)	Total (N=326)
Metabolism And Nutrition Disorders	56 (33.5%)	0	56 (17.2%)
Decreased Appetite	28 (16.8%)	0	28 (8.6%)
Hyperglycaemia	17 (10.2%)	0	17 (5.2%)
Infections And Infestations	44 (26.3%)	0	44 (13.5%)
Urinary Tract Infection	17 (10.2%)	0	17 (5.2%)
Blood And Lymphatic System Disorders	37 (22.2%)	0	37 (11.3%)
Anaemia	20 (12.0%)	0	20 (6.1%)
Neutropenia	13 (7.8%)	0	13 (4.0%)
Eye Disorders	32 (19.2%)	0	32 (9.8%)
Lacrimation Increased	13 (7.8%)	0	13 (4.0%)
Respiratory, Thoracic And Mediastinal Disorders	28 (16.8%)	0	28 (8.6%)
Renal And Urinary Disorders	23 (13.8%)	0	23 (7.1%)
Haematuria	10 (6.0%)	0	10 (3.1%)
Musculoskeletal And Connective Tissue Disorders	21 (12.6%)	0	21 (6.4%)
Endocrine Disorders	19 (11.4%)	0	19 (5.8%)
Hepatobiliary Disorders	14 (8.4%)	0	14 (4.3%)
Vascular Disorders	14 (8.4%)	0	14 (4.3%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are sorted by the descending number of patients in total group. In case of ties, alphabetical order is applied.
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2000.1.2.1: Frequency Summary of Treatment Emergent Adverse Events in Preoperative Phase
SAF2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=167)	RC + PLND (N=159)	Total (N=326)
Psychiatric Disorders	12 (7.2%)	0	12 (3.7%)
Cardiac Disorders	10 (6.0%)	0	10 (3.1%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are sorted by the descending number of patients in total group. In case of ties, alphabetical order is applied.
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2000.1.2.2: Frequency Summary of Treatment Emergent Adverse Events in Surgical Phase
SAF2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=167)	RC + PLND (N=159)	Total (N=326)
Overall	99 (59.3%)	103 (64.8%)	202 (62.0%)
Gastrointestinal Disorders	39 (23.4%)	45 (28.3%)	84 (25.8%)
Constipation	11 (6.6%)	13 (8.2%)	24 (7.4%)
Nausea	9 (5.4%)	12 (7.5%)	21 (6.4%)
Infections And Infestations	36 (21.6%)	48 (30.2%)	84 (25.8%)
Urinary Tract Infection	13 (7.8%)	20 (12.6%)	33 (10.1%)
Injury, Poisoning And Procedural Complications	26 (15.6%)	29 (18.2%)	55 (16.9%)
Procedural Pain	9 (5.4%)	12 (7.5%)	21 (6.4%)
Metabolism And Nutrition Disorders	22 (13.2%)	19 (11.9%)	41 (12.6%)
Blood And Lymphatic System Disorders	20 (12.0%)	19 (11.9%)	39 (12.0%)
Anaemia	20 (12.0%)	19 (11.9%)	39 (12.0%)
General Disorders And Administration Site Conditions	14 (8.4%)	22 (13.8%)	36 (11.0%)
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)	18 (10.8%)	15 (9.4%)	33 (10.1%)
Prostate Cancer	17 (10.2%)	15 (9.4%)	32 (9.8%)
Investigations	9 (5.4%)	15 (9.4%)	24 (7.4%)
Renal And Urinary Disorders	10 (6.0%)	14 (8.8%)	24 (7.4%)
Vascular Disorders	8 (4.8%)	12 (7.5%)	20 (6.1%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are sorted by the descending number of patients in total group. In case of ties, alphabetical order is applied.
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2000.1.2.2: Frequency Summary of Treatment Emergent Adverse Events in Surgical Phase
SAF2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=167)	RC + PLND (N=159)	Total (N=326)
Respiratory, Thoracic And Mediastinal Disorders	7 (4.2%)	12 (7.5%)	19 (5.8%)
Nervous System Disorders	13 (7.8%)	4 (2.5%)	17 (5.2%)
Psychiatric Disorders	7 (4.2%)	10 (6.3%)	17 (5.2%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are sorted by the descending number of patients in total group. In case of ties, alphabetical order is applied.
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2000.1.3: Frequency Summary of Treatment Emergent Adverse Events in Postoperative Phase
SAF2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=167)	RC + PLND (N=159)	Total (N=326)
Overall	99 (59.3%)	0	99 (30.4%)
Gastrointestinal Disorders	55 (32.9%)	0	55 (16.9%)
Diarrhoea	27 (16.2%)	0	27 (8.3%)
Constipation	15 (9.0%)	0	15 (4.6%)
Skin And Subcutaneous Tissue Disorders	50 (29.9%)	0	50 (15.3%)
Pruritus	28 (16.8%)	0	28 (8.6%)
Nervous System Disorders	43 (25.7%)	0	43 (13.2%)
Dysgeusia	14 (8.4%)	0	14 (4.3%)
Infections And Infestations	41 (24.6%)	0	41 (12.6%)
Urinary Tract Infection	15 (9.0%)	0	15 (4.6%)
Metabolism And Nutrition Disorders	40 (24.0%)	0	40 (12.3%)
Decreased Appetite	14 (8.4%)	0	14 (4.3%)
Investigations	35 (21.0%)	0	35 (10.7%)
Weight Decreased	11 (6.6%)	0	11 (3.4%)
General Disorders And Administration Site Conditions	33 (19.8%)	0	33 (10.1%)
Fatigue	11 (6.6%)	0	11 (3.4%)
Asthenia	10 (6.0%)	0	10 (3.1%)
Blood And Lymphatic System Disorders	26 (15.6%)	0	26 (8.0%)
Anaemia	14 (8.4%)	0	14 (4.3%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are sorted by the descending number of patients in total group. In case of ties, alphabetical order is applied.
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2000.1.3: Frequency Summary of Treatment Emergent Adverse Events in Postoperative Phase
SAF2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=167)	RC + PLND (N=159)	Total (N=326)
Musculoskeletal And Connective Tissue Disorders	18 (10.8%)	0	18 (5.5%)
Renal And Urinary Disorders	17 (10.2%)	0	17 (5.2%)
Eye Disorders	15 (9.0%)	0	15 (4.6%)
Injury, Poisoning And Procedural Complications	15 (9.0%)	0	15 (4.6%)
Respiratory, Thoracic And Mediastinal Disorders	15 (9.0%)	0	15 (4.6%)
Endocrine Disorders	14 (8.4%)	0	14 (4.3%)
Hypothyroidism	12 (7.2%)	0	12 (3.7%)
Psychiatric Disorders	10 (6.0%)	0	10 (3.1%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are sorted by the descending number of patients in total group. In case of ties, alphabetical order is applied.
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2000.2.1: Frequency Summary of Severe Treatment Emergent Adverse Events in Combined Treatment Phases
SAF2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=167)	RC + PLND (N=159)	Total (N=326)
Overall	120 (71.9%)	73 (45.9%)	193 (59.2%)
Infections And Infestations	55 (32.9%)	43 (27.0%)	98 (30.1%)
Urinary Tract Infection	20 (12.0%)	17 (10.7%)	37 (11.3%)
Gastrointestinal Disorders	31 (18.6%)	16 (10.1%)	47 (14.4%)
Blood And Lymphatic System Disorders	27 (16.2%)	10 (6.3%)	37 (11.3%)
Anaemia	15 (9.0%)	10 (6.3%)	25 (7.7%)
Neutropenia	10 (6.0%)	0	10 (3.1%)
Metabolism And Nutrition Disorders	26 (15.6%)	4 (2.5%)	30 (9.2%)
Renal And Urinary Disorders	19 (11.4%)	8 (5.0%)	27 (8.3%)
Skin And Subcutaneous Tissue Disorders	27 (16.2%)	0	27 (8.3%)
General Disorders And Administration Site Conditions	13 (7.8%)	10 (6.3%)	23 (7.1%)
Injury, Poisoning And Procedural Complications	10 (6.0%)	12 (7.5%)	22 (6.7%)
Investigations	16 (9.6%)	1 (0.6%)	17 (5.2%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are sorted by the descending number of patients in total group. In case of ties, alphabetical order is applied.
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2000.2.2.1: Frequency Summary of Severe Treatment Emergent Adverse Events in Preoperative Phase
SAF2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=167)	RC + PLND (N=159)	Total (N=326)
Overall	70 (41.9%)	0	70 (21.5%)
Skin And Subcutaneous Tissue Disorders	21 (12.6%)	0	21 (6.4%)
Blood And Lymphatic System Disorders	17 (10.2%)	0	17 (5.2%)
Metabolism And Nutrition Disorders	14 (8.4%)	0	14 (4.3%)
Infections And Infestations	13 (7.8%)	0	13 (4.0%)
Gastrointestinal Disorders	9 (5.4%)	0	9 (2.8%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are sorted by the descending number of patients in total group. In case of ties, alphabetical order is applied.
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2000.2.2.2: Frequency Summary of Severe Treatment Emergent Adverse Events in Surgical Phase
SAF2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=167)	RC + PLND (N=159)	Total (N=326)
Overall	53 (31.7%)	73 (45.9%)	126 (38.7%)
Infections And Infestations	25 (15.0%)	43 (27.0%)	68 (20.9%)
Urinary Tract Infection	8 (4.8%)	17 (10.7%)	25 (7.7%)
Gastrointestinal Disorders	11 (6.6%)	16 (10.1%)	27 (8.3%)
Injury, Poisoning And Procedural Complications	9 (5.4%)	12 (7.5%)	21 (6.4%)
Blood And Lymphatic System Disorders	7 (4.2%)	10 (6.3%)	17 (5.2%)
Anaemia	7 (4.2%)	10 (6.3%)	17 (5.2%)
Renal And Urinary Disorders	4 (2.4%)	8 (5.0%)	12 (3.7%)
General Disorders And Administration Site Conditions	1 (0.6%)	10 (6.3%)	11 (3.4%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are sorted by the descending number of patients in total group. In case of ties, alphabetical order is applied.
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2000.2.3: Frequency Summary of Severe Treatment Emergent Adverse Events in Postoperative Phase
SAF2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=167)	RC + PLND (N=159)	Total (N=326)
Overall	56 (33.5%)	0	56 (17.2%)
Infections And Infestations	22 (13.2%)	0	22 (6.7%)
Gastrointestinal Disorders	14 (8.4%)	0	14 (4.3%)
Investigations	9 (5.4%)	0	9 (2.8%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are sorted by the descending number of patients in total group. In case of ties, alphabetical order is applied.
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2000.3.1: Frequency Summary of Treatment Emergent Serious Adverse Events in Combined Treatment Phases
SAF2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=167)	RC + PLND (N=159)	Total (N=326)
Overall	98 (58.7%)	65 (40.9%)	163 (50.0%)
Infections And Infestations	49 (29.3%)	37 (23.3%)	86 (26.4%)
Urinary Tract Infection	17 (10.2%)	15 (9.4%)	32 (9.8%)
Gastrointestinal Disorders	21 (12.6%)	12 (7.5%)	33 (10.1%)
Renal And Urinary Disorders	19 (11.4%)	8 (5.0%)	27 (8.3%)
Injury, Poisoning And Procedural Complications	11 (6.6%)	7 (4.4%)	18 (5.5%)
General Disorders And Administration Site Conditions	9 (5.4%)	8 (5.0%)	17 (5.2%)
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)	9 (5.4%)	4 (2.5%)	13 (4.0%)
Skin And Subcutaneous Tissue Disorders	10 (6.0%)	0	10 (3.1%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are sorted by the descending number of patients in total group. In case of ties, alphabetical order is applied.
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2000.3.2.1: Frequency Summary of Treatment Emergent Serious Adverse Events in Preoperative Phase
SAF2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=167)	RC + PLND (N=159)	Total (N=326)
Overall	45 (26.9%)	0	45 (13.8%)
Infections And Infestations	12 (7.2%)	0	12 (3.7%)
Skin And Subcutaneous Tissue Disorders	10 (6.0%)	0	10 (3.1%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are sorted by the descending number of patients in total group. In case of ties, alphabetical order is applied.
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2000.3.2.2: Frequency Summary of Treatment Emergent Serious Adverse Events in Surgical Phase
SAF2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=167)	RC + PLND (N=159)	Total (N=326)
Overall	43 (25.7%)	65 (40.9%)	108 (33.1%)
Infections And Infestations	21 (12.6%)	37 (23.3%)	58 (17.8%)
Urinary Tract Infection	7 (4.2%)	15 (9.4%)	22 (6.7%)
Gastrointestinal Disorders	8 (4.8%)	12 (7.5%)	20 (6.1%)
Injury, Poisoning And Procedural Complications	10 (6.0%)	7 (4.4%)	17 (5.2%)
Renal And Urinary Disorders	6 (3.6%)	8 (5.0%)	14 (4.3%)
General Disorders And Administration Site Conditions	1 (0.6%)	8 (5.0%)	9 (2.8%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are sorted by the descending number of patients in total group. In case of ties, alphabetical order is applied.
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2000.3.3: Frequency Summary of Treatment Emergent Serious Adverse Events in Postoperative Phase
SAF2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=167)	RC + PLND (N=159)	Total (N=326)
Overall	43 (25.7%)	0	43 (13.2%)
Infections And Infestations	22 (13.2%)	0	22 (6.7%)
Gastrointestinal Disorders	9 (5.4%)	0	9 (2.8%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are sorted by the descending number of patients in total group. In case of ties, alphabetical order is applied.
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2000.4.1: Frequency Summary of Treatment Emergent Adverse Event Leading to Treatment Discontinuation in Combined Treatment Phases
SAF2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=167)	RC + PLND (N=159)	Total (N=326)
Overall	81 (48.5%)	0	81 (24.8%)
Skin And Subcutaneous Tissue Disorders	21 (12.6%)	0	21 (6.4%)
Pruritus	3 (1.8%)	0	3 (0.9%)
Rash	3 (1.8%)	0	3 (0.9%)
Dermatitis Exfoliative Generalised	2 (1.2%)	0	2 (0.6%)
Rash Maculo-Papular	2 (1.2%)	0	2 (0.6%)
Skin Exfoliation	2 (1.2%)	0	2 (0.6%)
Toxic Epidermal Necrolysis	2 (1.2%)	0	2 (0.6%)
Dermatitis	1 (0.6%)	0	1 (0.3%)
Dermatitis Bullous	1 (0.6%)	0	1 (0.3%)
Papule	1 (0.6%)	0	1 (0.3%)
Rash Vesicular	1 (0.6%)	0	1 (0.3%)
Toxic Erythema Of Chemotherapy	1 (0.6%)	0	1 (0.3%)
Toxic Skin Eruption	1 (0.6%)	0	1 (0.3%)
Urticaria	1 (0.6%)	0	1 (0.3%)
Nervous System Disorders	16 (9.6%)	0	16 (4.9%)
Peripheral Sensory Neuropathy	4 (2.4%)	0	4 (1.2%)
Neuropathy Peripheral	3 (1.8%)	0	3 (0.9%)
Dysgeusia	2 (1.2%)	0	2 (0.6%)
Neurotoxicity	2 (1.2%)	0	2 (0.6%)
Haemorrhage Intracranial	1 (0.6%)	0	1 (0.3%)
Myasthenia Gravis	1 (0.6%)	0	1 (0.3%)
Paraesthesia	1 (0.6%)	0	1 (0.3%)
Peripheral Motor Neuropathy	1 (0.6%)	0	1 (0.3%)
Polyneuropathy	1 (0.6%)	0	1 (0.3%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are sorted by the descending number of patients in total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2000.4.1: Frequency Summary of Treatment Emergent Adverse Event Leading to Treatment Discontinuation in Combined Treatment Phases
SAF2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=167)	RC + PLND (N=159)	Total (N=326)
Gastrointestinal Disorders	12 (7.2%)	0	12 (3.7%)
Diarrhoea	7 (4.2%)	0	7 (2.1%)
Intestinal Obstruction	2 (1.2%)	0	2 (0.6%)
Colitis	1 (0.6%)	0	1 (0.3%)
Immune-Mediated Enterocolitis	1 (0.6%)	0	1 (0.3%)
Small Intestinal Obstruction	1 (0.6%)	0	1 (0.3%)
Infections And Infestations	7 (4.2%)	0	7 (2.1%)
Sepsis	2 (1.2%)	0	2 (0.6%)
Bacterial Infection	1 (0.6%)	0	1 (0.3%)
Endocarditis	1 (0.6%)	0	1 (0.3%)
Eye Infection	1 (0.6%)	0	1 (0.3%)
Urinary Tract Infection	1 (0.6%)	0	1 (0.3%)
Urosepsis	1 (0.6%)	0	1 (0.3%)
Investigations	6 (3.6%)	0	6 (1.8%)
Alanine Aminotransferase Increased	3 (1.8%)	0	3 (0.9%)
Aspartate Aminotransferase Increased	3 (1.8%)	0	3 (0.9%)
Amylase Increased	1 (0.6%)	0	1 (0.3%)
Blood Creatine Phosphokinase Increased	1 (0.6%)	0	1 (0.3%)
Blood Creatinine Increased	1 (0.6%)	0	1 (0.3%)
Glomerular Filtration Rate Decreased	1 (0.6%)	0	1 (0.3%)
Renal And Urinary Disorders	6 (3.6%)	0	6 (1.8%)
Acute Kidney Injury	2 (1.2%)	0	2 (0.6%)
Autoimmune Nephritis	1 (0.6%)	0	1 (0.3%)
Nephritis	1 (0.6%)	0	1 (0.3%)
Renal Impairment	1 (0.6%)	0	1 (0.3%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are sorted by the descending number of patients in total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2000.4.1: Frequency Summary of Treatment Emergent Adverse Event Leading to Treatment Discontinuation in Combined Treatment Phases
SAF2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=167)	RC + PLND (N=159)	Total (N=326)
Tubulointerstitial Nephritis	1 (0.6%)	0	1 (0.3%)
General Disorders And Administration Site Conditions	4 (2.4%)	0	4 (1.2%)
Fatigue	2 (1.2%)	0	2 (0.6%)
Death	1 (0.6%)	0	1 (0.3%)
Multiple Organ Dysfunction Syndrome	1 (0.6%)	0	1 (0.3%)
Respiratory, Thoracic And Mediastinal Disorders	4 (2.4%)	0	4 (1.2%)
Pneumonitis	3 (1.8%)	0	3 (0.9%)
Respiratory Distress	1 (0.6%)	0	1 (0.3%)
Cardiac Disorders	3 (1.8%)	0	3 (0.9%)
Acute Myocardial Infarction	1 (0.6%)	0	1 (0.3%)
Myocardial Infarction	1 (0.6%)	0	1 (0.3%)
Myocarditis	1 (0.6%)	0	1 (0.3%)
Hepatobiliary Disorders	3 (1.8%)	0	3 (0.9%)
Hepatic Function Abnormal	1 (0.6%)	0	1 (0.3%)
Hepatitis	1 (0.6%)	0	1 (0.3%)
Hypertransaminasaemia	1 (0.6%)	0	1 (0.3%)
Metabolism And Nutrition Disorders	2 (1.2%)	0	2 (0.6%)
Diabetes Mellitus	1 (0.6%)	0	1 (0.3%)
Hypokalaemia	1 (0.6%)	0	1 (0.3%)
Musculoskeletal And Connective Tissue Disorders	2 (1.2%)	0	2 (0.6%)
Arthralgia	2 (1.2%)	0	2 (0.6%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are sorted by the descending number of patients in total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2000.4.1: Frequency Summary of Treatment Emergent Adverse Event Leading to Treatment Discontinuation in Combined Treatment Phases
SAF2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=167)	RC + PLND (N=159)	Total (N=326)
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)	2 (1.2%)	0	2 (0.6%)
Bile Duct Cancer	1 (0.6%)	0	1 (0.3%)
Colon Cancer	1 (0.6%)	0	1 (0.3%)
Blood And Lymphatic System Disorders	1 (0.6%)	0	1 (0.3%)
Anaemia	1 (0.6%)	0	1 (0.3%)
Injury, Poisoning And Procedural Complications	1 (0.6%)	0	1 (0.3%)
Road Traffic Accident	1 (0.6%)	0	1 (0.3%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are sorted by the descending number of patients in total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2000.4.2.1: Frequency Summary of Treatment Emergent Adverse Event Leading to Treatment Discontinuation in Preoperative Phase
SAF2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=167)	RC + PLND (N=159)	Total (N=326)
Overall	38 (22.8%)	0	38 (11.7%)
Skin And Subcutaneous Tissue Disorders	15 (9.0%)	0	15 (4.6%)
Dermatitis Exfoliative Generalised	2 (1.2%)	0	2 (0.6%)
Pruritus	2 (1.2%)	0	2 (0.6%)
Rash	2 (1.2%)	0	2 (0.6%)
Skin Exfoliation	2 (1.2%)	0	2 (0.6%)
Toxic Epidermal Necrolysis	2 (1.2%)	0	2 (0.6%)
Dermatitis	1 (0.6%)	0	1 (0.3%)
Papule	1 (0.6%)	0	1 (0.3%)
Rash Maculo-Papular	1 (0.6%)	0	1 (0.3%)
Toxic Erythema Of Chemotherapy	1 (0.6%)	0	1 (0.3%)
Toxic Skin Eruption	1 (0.6%)	0	1 (0.3%)
Nervous System Disorders	7 (4.2%)	0	7 (2.1%)
Dysgeusia	2 (1.2%)	0	2 (0.6%)
Peripheral Sensory Neuropathy	2 (1.2%)	0	2 (0.6%)
Myasthenia Gravis	1 (0.6%)	0	1 (0.3%)
Paraesthesia	1 (0.6%)	0	1 (0.3%)
Peripheral Motor Neuropathy	1 (0.6%)	0	1 (0.3%)
Gastrointestinal Disorders	3 (1.8%)	0	3 (0.9%)
Diarrhoea	2 (1.2%)	0	2 (0.6%)
Intestinal Obstruction	1 (0.6%)	0	1 (0.3%)
Hepatobiliary Disorders	3 (1.8%)	0	3 (0.9%)
Hepatic Function Abnormal	1 (0.6%)	0	1 (0.3%)
Hepatitis	1 (0.6%)	0	1 (0.3%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are sorted by the descending number of patients in total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2000.4.2.1: Frequency Summary of Treatment Emergent Adverse Event Leading to Treatment Discontinuation in Preoperative Phase SAF2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=167)	RC + PLND (N=159)	Total (N=326)
Hypertransaminasaemia	1 (0.6%)	0	1 (0.3%)
Investigations	3 (1.8%)	0	3 (0.9%)
Alanine Aminotransferase Increased	2 (1.2%)	0	2 (0.6%)
Aspartate Aminotransferase Increased	2 (1.2%)	0	2 (0.6%)
Blood Creatine Phosphokinase Increased	1 (0.6%)	0	1 (0.3%)
Blood Creatinine Increased	1 (0.6%)	0	1 (0.3%)
Cardiac Disorders	2 (1.2%)	0	2 (0.6%)
Acute Myocardial Infarction	1 (0.6%)	0	1 (0.3%)
Myocarditis	1 (0.6%)	0	1 (0.3%)
General Disorders And Administration Site Conditions	2 (1.2%)	0	2 (0.6%)
Fatigue	2 (1.2%)	0	2 (0.6%)
Infections And Infestations	2 (1.2%)	0	2 (0.6%)
Endocarditis	1 (0.6%)	0	1 (0.3%)
Urinary Tract Infection	1 (0.6%)	0	1 (0.3%)
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)	2 (1.2%)	0	2 (0.6%)
Bile Duct Cancer	1 (0.6%)	0	1 (0.3%)
Colon Cancer	1 (0.6%)	0	1 (0.3%)
Respiratory, Thoracic And Mediastinal Disorders	2 (1.2%)	0	2 (0.6%)
Pneumonitis	1 (0.6%)	0	1 (0.3%)
Respiratory Distress	1 (0.6%)	0	1 (0.3%)
Metabolism And Nutrition Disorders	1 (0.6%)	0	1 (0.3%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are sorted by the descending number of patients in total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2000.4.2.1: Frequency Summary of Treatment Emergent Adverse Event Leading to Treatment Discontinuation in Preoperative Phase
SAF2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=167)	RC + PLND (N=159)	Total (N=326)
Diabetes Mellitus	1 (0.6%)	0	1 (0.3%)
Musculoskeletal And Connective Tissue Disorders	1 (0.6%)	0	1 (0.3%)
Arthralgia	1 (0.6%)	0	1 (0.3%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are sorted by the descending number of patients in total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2000.4.2.2: Frequency Summary of Treatment Emergent Adverse Event Leading to Treatment Discontinuation in Surgical Phase SAF2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=167)	RC + PLND (N=159)	Total (N=326)
Overall	5 (3.0%)	0	5 (1.5%)
Infections And Infestations	2 (1.2%)	0	2 (0.6%)
Bacterial Infection	1 (0.6%)	0	1 (0.3%)
Sepsis	1 (0.6%)	0	1 (0.3%)
Gastrointestinal Disorders	1 (0.6%)	0	1 (0.3%)
Colitis	1 (0.6%)	0	1 (0.3%)
Nervous System Disorders	1 (0.6%)	0	1 (0.3%)
Peripheral Sensory Neuropathy	1 (0.6%)	0	1 (0.3%)
Renal And Urinary Disorders	1 (0.6%)	0	1 (0.3%)
Renal Impairment	1 (0.6%)	0	1 (0.3%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are sorted by the descending number of patients in total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2000.4.3: Frequency Summary of Treatment Emergent Adverse Event Leading to Treatment Discontinuation in Postoperative Phase
SAF2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=167)	RC + PLND (N=159)	Total (N=326)
Overall	37 (22.2%)	0	37 (11.3%)
Gastrointestinal Disorders	8 (4.8%)	0	8 (2.5%)
Diarrhoea	5 (3.0%)	0	5 (1.5%)
Immune-Mediated Enterocolitis	1 (0.6%)	0	1 (0.3%)
Intestinal Obstruction	1 (0.6%)	0	1 (0.3%)
Small Intestinal Obstruction	1 (0.6%)	0	1 (0.3%)
Nervous System Disorders	7 (4.2%)	0	7 (2.1%)
Neuropathy Peripheral	2 (1.2%)	0	2 (0.6%)
Neurotoxicity	2 (1.2%)	0	2 (0.6%)
Haemorrhage Intracranial	1 (0.6%)	0	1 (0.3%)
Peripheral Sensory Neuropathy	1 (0.6%)	0	1 (0.3%)
Polyneuropathy	1 (0.6%)	0	1 (0.3%)
Skin And Subcutaneous Tissue Disorders	6 (3.6%)	0	6 (1.8%)
Dermatitis Bullous	1 (0.6%)	0	1 (0.3%)
Pruritus	1 (0.6%)	0	1 (0.3%)
Rash	1 (0.6%)	0	1 (0.3%)
Rash Maculo-Papular	1 (0.6%)	0	1 (0.3%)
Rash Vesicular	1 (0.6%)	0	1 (0.3%)
Urticaria	1 (0.6%)	0	1 (0.3%)
Renal And Urinary Disorders	5 (3.0%)	0	5 (1.5%)
Acute Kidney Injury	2 (1.2%)	0	2 (0.6%)
Autoimmune Nephritis	1 (0.6%)	0	1 (0.3%)
Nephritis	1 (0.6%)	0	1 (0.3%)
Tubulointerstitial Nephritis	1 (0.6%)	0	1 (0.3%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are sorted by the descending number of patients in total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2000.4.3: Frequency Summary of Treatment Emergent Adverse Event Leading to Treatment Discontinuation in Postoperative Phase
SAF2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=167)	RC + PLND (N=159)	Total (N=326)
Infections And Infestations	3 (1.8%)	0	3 (0.9%)
Eye Infection	1 (0.6%)	0	1 (0.3%)
Sepsis	1 (0.6%)	0	1 (0.3%)
Urosepsis	1 (0.6%)	0	1 (0.3%)
Investigations	3 (1.8%)	0	3 (0.9%)
Alanine Aminotransferase Increased	1 (0.6%)	0	1 (0.3%)
Amylase Increased	1 (0.6%)	0	1 (0.3%)
Aspartate Aminotransferase Increased	1 (0.6%)	0	1 (0.3%)
Glomerular Filtration Rate Decreased	1 (0.6%)	0	1 (0.3%)
General Disorders And Administration Site Conditions	2 (1.2%)	0	2 (0.6%)
Death	1 (0.6%)	0	1 (0.3%)
Multiple Organ Dysfunction Syndrome	1 (0.6%)	0	1 (0.3%)
Respiratory, Thoracic And Mediastinal Disorders	2 (1.2%)	0	2 (0.6%)
Pneumonitis	2 (1.2%)	0	2 (0.6%)
Cardiac Disorders	1 (0.6%)	0	1 (0.3%)
Myocardial Infarction	1 (0.6%)	0	1 (0.3%)
Injury, Poisoning And Procedural Complications	1 (0.6%)	0	1 (0.3%)
Road Traffic Accident	1 (0.6%)	0	1 (0.3%)
Metabolism And Nutrition Disorders	1 (0.6%)	0	1 (0.3%)
Hypokalaemia	1 (0.6%)	0	1 (0.3%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are sorted by the descending number of patients in total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2000.4.3: Frequency Summary of Treatment Emergent Adverse Event Leading to Treatment Discontinuation in Postoperative Phase
SAF2 Analysis Set

MedDRA SOC and PT	EV + Pembro (N=167)	RC + PLND (N=159)	Total (N=326)
Musculoskeletal And Connective Tissue Disorders	1 (0.6%)	0	1 (0.3%)
Arthralgia	1 (0.6%)	0	1 (0.3%)

Abbreviations: EV=enfortumab vedotin; N=number of patients; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are sorted by the descending number of patients in total group. In case of ties, alphabetical order is applied.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2000.5.1: Summary of Duration of Observation Time for Treatment Emergent Adverse Events in Combined Treatment Phases
SAF2 Analysis Set

	EV + Pembro (N=167)	**RC + PLND (N=159)**
Duration of observation period (months)		
n	167	159
Mean (SD)	8.6 (5.23)	1.0 (0.08)
Median	7.3	1.0
Q1 - Q3	3.7 - 14.3	1.0 - 1.0
Min - Max	1.0 - 20.7	0.4 - 1.0

Abbreviations: DCO=data cut-off; EV=enfortumab vedotin; Max=maximum; Min=minimum; N=number of patients; n=number of patients with non-missing values; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; Q1=first quartile; Q3=third quartile; RC=radical cystectomy; SD=standard deviation.
Observation time for treatment emergent adverse events is defined as the time from first dose until DCO, study treatment discontinuation +30 days or death, whichever occurred first and stopped the collection of endpoint data.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2000.5.2: Summary of Duration of Observation Time for Treatment Emergent Adverse Events in Surgical Phase
SAF2 Analysis Set

	EV + Pembro (N=167)	**RC + PLND (N=159)**
Duration of observation period (months)		
n	146	159
Mean (SD)	1.8 (0.70)	1.0 (0.08)
Median	1.8	1.0
Q1 - Q3	1.0 - 2.1	1.0 - 1.0
Min - Max	0.2 - 4.8	0.4 - 1.0

Abbreviations: DCO=data cut-off; EV=enfortumab vedotin; Max=maximum; Min=minimum; N=number of patients; n=number of patients with non-missing values; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; Q1=first quartile; Q3=third quartile; RC=radical cystectomy; SD=standard deviation.
Observation time for the surgical phase is defined as the time from surgery until date of first postoperative treatment or, if there was no postoperative treatment, surgery date +30 days or death, whichever occurred first.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2000.6.1: Summary of Duration of Observation Time for Treatment Emergent Serious Adverse Events in Combined Treatment Phases
SAF2 Analysis Set

	EV + Pembro (N=167)	**RC + PLND (N=159)**
Duration of observation period (months)		
n	167	159
Mean (SD)	10.2 (5.15)	2.9 (0.42)
Median	9.0	3.0
Q1 - Q3	5.7 - 15.4	3.0 - 3.0
Min - Max	1.3 - 22.7	0.4 - 3.0

Abbreviations: DCO=data cut-off; EV=enfortumab vedotin; Max=maximum; Min=minimum; N=number of patients; n=number of patients with non-missing values; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; Q1=first quartile; Q3=third quartile; RC=radical cystectomy; SD=standard deviation.
Observation time for treatment emergent serious adverse events is defined as the time from first dose until DCO, study treatment discontinuation +90 days or death, whichever occurred first and stopped the collection of endpoint data.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2000.6.2: Summary of Duration of Observation Time for Treatment Emergent Serious Adverse Events in Surgical Phase
SAF2 Analysis Set

	EV + Pembro (N=167)	RC + PLND (N=159)
Duration of observation period (months)		
n	146	159
Mean (SD)	2.3 (0.66)	2.9 (0.42)
Median	2.1	3.0
Q1 - Q3	1.8 - 3.0	3.0 - 3.0
Min - Max	0.2 - 4.8	0.4 - 3.0

Abbreviations: DCO=data cut-off; EV=enfortumab vedotin; Max=maximum; Min=minimum; N=number of patients; n=number of patients with non-missing values; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; Q1=first quartile; Q3=third quartile; RC=radical cystectomy; SD=standard deviation.
Observation time for the surgical phase is defined as the time from surgery until date of first postoperative treatment or, if there was no postoperative treatment, surgery date +90 days or death, whichever occurred first.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Endpunkt: Unerwünschte Ereignisse; Ereigniszeitanalysen, Tabellen

Table 303.1.2001.1.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	167 (100.0%)	103 (64.8%)	
Number of patients censored	0 (0.0%)	56 (35.2%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	0.26 [0.20, 0.26]	0.46 [0.16, 1.02]	
Difference in median			-0.20
Cox proportional hazards model			
Unstratified HR, 95% CI			1.714 [1.329, 2.210]
Log-rank test			
Two-sided unstratified log-rank p-value			<.0001

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.1.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	138 (100.0)	0.26 [0.20, 0.26]	129	85 (65.9)	0.39 [0.13, 1.02]	1.664 [1.258, 2.202]	0.0002	0.5001
Eligible but Declined	29	29 (100.0)	0.26 [0.10, 0.33]	30	18 (60.0)	0.69 [0.03, NC]	2.020 [1.091, 3.741]	0.0145	
Tumor Stage									
T2N0	31	31 (100.0)	0.16 [0.07, 0.26]	27	13 (48.1)	1.15 [0.13, NC]	2.509 [1.280, 4.920]	0.0047	0.1928
T3/T4aN0	129	129 (100.0)	0.26 [0.23, 0.30]	125	86 (68.8)	0.30 [0.13, 0.92]	1.568 [1.183, 2.079]	0.0008	
T1-4aN1	7	7 (100.0)	0.10 [0.03, 0.46]	7	4 (57.1)	0.07 [0.03, NC]	1.709 [0.487, 6.003]	0.3244	
Geographical Regions									
US	21	21 (100.0)	0.07 [0.03, 0.20]	23	18 (78.3)	0.07 [0.03, 0.46]	1.567 [0.803, 3.058]	0.1041	0.7376
EU	76	76 (100.0)	0.26 [0.16, 0.26]	69	48 (69.6)	0.26 [0.07, 1.02]	1.574 [1.082, 2.290]	0.0105	
MOW	70	70 (100.0)	0.30 [0.23, 0.43]	67	37 (55.2)	1.08 [0.36, 1.81]	2.003 [1.326, 3.026]	0.0006	
Age Category									
< 65	29	29 (100.0)	0.33 [0.20, 0.66]	28	16 (57.1)	1.20 [0.10, NC]	2.457 [1.295, 4.662]	0.0035	0.5327
>= 65	138	138 (100.0)	0.23 [0.16, 0.26]	131	87 (66.4)	0.30 [0.13, 1.02]	1.615 [1.223, 2.133]	0.0003	
Sex									
Male	135	135 (100.0)	0.26 [0.23, 0.30]	120	77 (64.2)	0.25 [0.07, 1.02]	1.481 [1.109, 1.977]	0.0036	0.0400
Female	32	32 (100.0)	0.16 [0.10, 0.30]	39	26 (66.7)	1.02 [0.26, 1.41]	4.352 [2.316, 8.177]	<.0001	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.2.1.1: Time to Event Analysis of Severe Treatment Emergent Adverse Events in Combined Treatment Phases
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	120 (71.9%)	73 (45.9%)	
Number of patients censored	47 (28.1%)	86 (54.1%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	2.96 [2.66, 3.61]	1.38 [1.15, 1.41]	
Difference in median			1.58
Cox proportional hazards model			
Unstratified HR, 95% CI			0.530 [0.370, 0.761]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0005

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.2.1.2: Time to Event Analysis of Severe Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	100 (72.5)	2.96 [2.60, 3.61]	129	65 (50.4)	1.25 [1.08, 1.41]	0.487 [0.331, 0.717]	0.0002	0.2831
Eligible but Declined	29	20 (69.0)	3.48 [1.12, 10.84]	30	8 (26.7)	2.00 [2.00, NC]	0.854 [0.312, 2.340]	0.7641	
Tumor Stage									
T2N0	31	23 (74.2)	2.76 [1.08, 5.62]	27	9 (33.3)	1.41 [1.15, NC]	0.654 [0.246, 1.740]	0.4055	0.2512
T3/T4aN0	129	92 (71.3)	3.12 [2.66, 4.14]	125	61 (48.8)	1.38 [1.08, 1.61]	0.516 [0.347, 0.769]	0.0010	
T1-4aN1	7	5 (71.4)	2.53 [0.26, NC]	7	3 (42.9)	1.91 [0.23, NC]	0.594 [0.114, 3.104]	0.5335	
Geographical Regions									
US	21	16 (76.2)	2.76 [0.62, 3.09]	23	11 (47.8)	1.38 [0.59, NC]	0.588 [0.227, 1.520]	0.2761	0.8398
EU	76	55 (72.4)	3.15 [1.38, 4.63]	69	35 (50.7)	1.25 [1.02, 1.61]	0.491 [0.293, 0.825]	0.0064	
MOW	70	49 (70.0)	3.12 [2.53, 5.85]	67	27 (40.3)	1.41 [1.08, 2.43]	0.579 [0.322, 1.042]	0.0643	
Age Category									
< 65	29	18 (62.1)	4.11 [2.66, NC]	28	11 (39.3)	2.00 [1.38, NC]	0.268 [0.088, 0.814]	0.0158	0.6893
>= 65	138	102 (73.9)	2.86 [1.64, 3.52]	131	62 (47.3)	1.25 [1.08, 1.41]	0.573 [0.391, 0.840]	0.0042	
Sex									
Male	135	97 (71.9)	2.96 [2.17, 4.11]	120	52 (43.3)	1.38 [1.15, 1.61]	0.598 [0.397, 0.900]	0.0132	0.9190
Female	32	23 (71.9)	2.86 [0.85, 5.78]	39	21 (53.8)	1.41 [0.95, 1.81]	0.336 [0.148, 0.764]	0.0071	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.3.1.1: Time to Event Analysis of Treatment Emergent Serious Adverse Events in Combined Treatment Phases
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	98 (58.7%)	65 (40.9%)	
Number of patients censored	69 (41.3%)	94 (59.1%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	5.88 [4.11, 8.05]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.694 [0.484, 0.995]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0470

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 90 days, death date).
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.3.1.2: Time to Event Analysis of Treatment Emergent Serious Adverse Events in Combined Treatment Phases by Subgroups
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	84 (60.9)	5.26 [3.61, 7.56]	129	57 (44.2)	NC [1.94, NC]	0.658 [0.446, 0.971]	0.0346	0.7416
Eligible but Declined	29	14 (48.3)	12.22 [3.98, NC]	30	8 (26.7)	NC [NC, NC]	0.939 [0.352, 2.501]	0.8983	
Tumor Stage									
T2N0	31	17 (54.8)	5.85 [3.09, NC]	27	8 (29.6)	NC [1.41, NC]	0.903 [0.348, 2.341]	0.8382	0.6667
T3/T4aN0	129	77 (59.7)	5.68 [3.52, 10.38]	125	54 (43.2)	NC [2.56, NC]	0.707 [0.476, 1.050]	0.0864	
T1-4aN1	7	4 (57.1)	7.92 [3.68, NC]	7	3 (42.9)	NC [0.23, NC]	0.000 [0.000, NC]	0.0597	
Geographical Regions									
US	21	13 (61.9)	7.98 [2.66, 13.83]	23	11 (47.8)	NC [0.76, NC]	0.621 [0.249, 1.547]	0.3021	0.4370
EU	76	43 (56.6)	6.74 [3.52, 13.37]	69	31 (44.9)	NC [1.41, NC]	0.517 [0.297, 0.900]	0.0182	
MOW	70	42 (60.0)	5.68 [3.68, 13.70]	67	23 (34.3)	NC [NC, NC]	0.988 [0.561, 1.741]	0.9707	
Age Category									
< 65	29	17 (58.6)	5.98 [3.22, NC]	28	12 (42.9)	NC [1.38, NC]	0.460 [0.181, 1.169]	0.0946	0.6042
>= 65	138	81 (58.7)	5.88 [3.71, 8.05]	131	53 (40.5)	NC [NC, NC]	0.748 [0.505, 1.108]	0.1490	
Sex									
Male	135	83 (61.5)	5.68 [3.61, 7.92]	120	46 (38.3)	NC [NC, NC]	0.815 [0.543, 1.224]	0.3310	0.1281
Female	32	15 (46.9)	9.79 [3.71, NC]	39	19 (48.7)	NC [1.08, NC]	0.361 [0.152, 0.861]	0.0168	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 90 days, death date).
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.4.1.1: Time to Event Analysis of Treatment Emergent Adverse Events leading to Treatment Discontinuation in Combined Treatment Phases
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	81 (48.5%)	0 (0.0%)	
Number of patients censored	86 (51.5%)	159 (100.0%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	8.34 [6.77, 14.06]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			NC [NC, NC]
Log-rank test			
Two-sided unstratified log-rank p-value			<.0001

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.4.1.2: Time to Event Analysis of Treatment Emergent Adverse Events leading to Treatment Discontinuation in Combined Treatment Phases by Subgroups
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	64 (46.4)	8.34 [6.24, NC]	129	0 (0.0)	NC [NC, NC]	NC [NC, NC]	<.0001	1.0000
Eligible but Declined	29	17 (58.6)	8.67 [6.21, 12.22]	30	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.1467	
Tumor Stage									
T2N0	31	16 (51.6)	6.24 [2.86, NC]	27	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0308	1.0000
T3/T4aN0	129	64 (49.6)	8.11 [6.47, 14.06]	125	0 (0.0)	NC [NC, NC]	NC [NC, NC]	<.0001	
T1-4aN1	7	1 (14.3)	NC [6.90, NC]	7	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	
Geographical Regions									
US	21	10 (47.6)	8.90 [5.45, NC]	23	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	1.0000
EU	76	43 (56.6)	7.00 [4.70, 12.16]	69	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0002	
MOW	70	28 (40.0)	8.34 [6.77, NC]	67	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0027	
Age Category									
< 65	29	11 (37.9)	NC [7.62, NC]	28	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	0.9997
>= 65	138	70 (50.7)	7.36 [6.21, 10.94]	131	0 (0.0)	NC [NC, NC]	NC [NC, NC]	<.0001	
Sex									
Male	135	66 (48.9)	8.67 [6.47, NC]	120	0 (0.0)	NC [NC, NC]	NC [NC, NC]	<.0001	1.0000
Female	32	15 (46.9)	7.56 [4.57, NC]	39	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0551	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.5.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Blood and Lymphatic System Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	69 (41.3%)	19 (11.9%)	
Number of patients censored	98 (58.7%)	140 (88.1%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	10.81 [6.83, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			1.311 [0.729, 2.358]
Log-rank test			
Two-sided unstratified log-rank p-value			0.3613

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.6.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Anaemia (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	51 (30.5%)	19 (11.9%)	
Number of patients censored	116 (69.5%)	140 (88.1%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	17.38 [17.38, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.520 [0.247, 1.093]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0786

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.7.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Neutropenia (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	16 (9.6%)	0 (0.0%)	
Number of patients censored	151 (90.4%)	159 (100.0%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			NC [NC, NC]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0033

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.7.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Neutropenia (PT)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	13 (9.4)	NC [NC, NC]	129	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0061	1.0000
Eligible but Declined	29	3 (10.3)	NC [NC, NC]	30	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.3091	
Tumor Stage									
T2N0	31	1 (3.2)	NC [NC, NC]	27	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.3507	1.0000
T3/T4aN0	129	13 (10.1)	NC [NC, NC]	125	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0091	
T1-4aN1	7	2 (28.6)	NC [0.69, NC]	7	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.3173	
Geographical Regions									
US	21	1 (4.8)		23	0 (0.0)				
EU	76	8 (10.5)		69	0 (0.0)				
MOW	70	7 (10.0)		67	0 (0.0)				
Age Category									
< 65	29	2 (6.9)	NC [NC, NC]	28	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.3258	0.9999
>= 65	138	14 (10.1)	NC [NC, NC]	131	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0058	
Sex									
Male	135	11 (8.1)	NC [NC, NC]	120	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0349	0.9998
Female	32	5 (15.6)	NC [NC, NC]	39	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0255	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.8.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Cardiac Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	17 (10.2%)	6 (3.8%)	
Number of patients censored	150 (89.8%)	153 (96.2%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	2.04 [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.481 [0.124, 1.868]
Log-rank test			
Two-sided unstratified log-rank p-value			0.2819

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.9.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Endocrine Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	33 (19.8%)	0 (0.0%)	
Number of patients censored	134 (80.2%)	159 (100.0%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			NC [NC, NC]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0058

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.9.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Endocrine Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	28 (20.3)	NC [NC, NC]	129	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0062	0.9999
Eligible but Declined	29	5 (17.2)	NC [13.44, NC]	30	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	
Tumor Stage									
T2N0	31	9 (29.0)	14.98 [9.00, NC]	27	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.3507	1.0000
T3/T4aN0	129	22 (17.1)	NC [NC, NC]	125	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0288	
T1-4aN1	7	2 (28.6)	NC [0.26, NC]	7	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.1413	
Geographical Regions									
US	21	5 (23.8)	13.44 [6.80, NC]	23	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.3061	1.0000
EU	76	15 (19.7)	NC [NC, NC]	69	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0308	
MOW	70	13 (18.6)	NC [14.98, NC]	67	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.1747	
Age Category									
< 65	29	5 (17.2)	NC [NC, NC]	28	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.3258	0.9999
>= 65	138	28 (20.3)	NC [14.98, NC]	131	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0100	
Sex									
Male	135	26 (19.3)	NC [NC, NC]	120	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0205	0.9999
Female	32	7 (21.9)	14.98 [9.00, NC]	39	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.1255	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.10.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Hypothyroidism (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	24 (14.4%)	0 (0.0%)	
Number of patients censored	143 (85.6%)	159 (100.0%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			NC [NC, NC]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0928

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.11.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Eye Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	41 (24.6%)	0 (0.0%)	
Number of patients censored	126 (75.4%)	159 (100.0%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			NC [NC, NC]
Log-rank test			
Two-sided unstratified log-rank p-value			<.0001

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.11.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Eye Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	29 (21.0)	NC [NC, NC]	129	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0004	0.9997
Eligible but Declined	29	12 (41.4)	NC [1.61, NC]	30	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0183	
Tumor Stage									
T2N0	31	9 (29.0)	NC [5.16, NC]	27	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.1003	1.0000
T3/T4aN0	129	31 (24.0)	NC [NC, NC]	125	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0002	
T1-4aN1	7	1 (14.3)	NC [0.76, NC]	7	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.3173	
Geographical Regions									
US	21	9 (42.9)	NC [1.08, NC]	23	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0151	1.0000
EU	76	24 (31.6)	NC [9.46, NC]	69	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0011	
MOW	70	8 (11.4)	NC [NC, NC]	67	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.1747	
Age Category									
< 65	29	4 (13.8)	NC [NC, NC]	28	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	0.9996
>= 65	138	37 (26.8)	NC [NC, NC]	131	0 (0.0)	NC [NC, NC]	NC [NC, NC]	<.0001	
Sex									
Male	135	33 (24.4)	NC [NC, NC]	120	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0003	0.9999
Female	32	8 (25.0)	NC [11.93, NC]	39	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0246	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.12.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Dry Eye (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	10 (6.0%)	0 (0.0%)	
Number of patients censored	157 (94.0%)	159 (100.0%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			NC [NC, NC]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0171

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.12.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Dry Eye (PT)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	8 (5.8)		129	0 (0.0)				
Eligible but Declined	29	2 (6.9)		30	0 (0.0)				
Tumor Stage									
T2N0	31	4 (12.9)		27	0 (0.0)				
T3/T4aN0	129	6 (4.7)		125	0 (0.0)				
T1-4aN1	7	0 (0.0)		7	0 (0.0)				
Geographical Regions									
US	21	0 (0.0)		23	0 (0.0)				
EU	76	9 (11.8)		69	0 (0.0)				
MOW	70	1 (1.4)		67	0 (0.0)				
Age Category									
< 65	29	0 (0.0)	NC [NC, NC]	28	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	0.9980
>= 65	138	10 (7.2)	NC [NC, NC]	131	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0173	
Sex									
Male	135	9 (6.7)		120	0 (0.0)				
Female	32	1 (3.1)		39	0 (0.0)				

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.13.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Lacrimation Increased (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	16 (9.6%)	0 (0.0%)	
Number of patients censored	151 (90.4%)	159 (100.0%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			NC [NC, NC]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0514

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.14.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Gastrointestinal Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	118 (70.7%)	45 (28.3%)	
Number of patients censored	49 (29.3%)	114 (71.7%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	2.56 [1.41, 3.12]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			1.257 [0.855, 1.848]
Log-rank test			
Two-sided unstratified log-rank p-value			0.2353

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.15.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Abdominal Pain (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	17 (10.2%)	9 (5.7%)	
Number of patients censored	150 (89.8%)	150 (94.3%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.204 [0.044, 0.943]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0242

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.15.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Abdominal Pain (PT)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	13 (9.4)	NC [NC, NC]	129	7 (5.4)	NC [NC, NC]	0.257 [0.053, 1.236]	0.0674	0.9331
Eligible but Declined	29	4 (13.8)	NC [NC, NC]	30	2 (6.7)	NC [NC, NC]	0.000 [0.000, NC]	0.1607	
Tumor Stage									
T2N0	31	4 (12.9)	NC [NC, NC]	27	2 (7.4)	NC [NC, NC]	0.419 [0.038, 4.623]	0.4638	0.7835
T3/T4aN0	129	11 (8.5)	NC [NC, NC]	125	5 (4.0)	NC [NC, NC]	0.188 [0.022, 1.607]	0.0871	
T1-4aN1	7	2 (28.6)	11.86 [3.09, NC]	7	2 (28.6)	NC [0.03, NC]	0.000 [0.000, NC]	0.1413	
Geographical Regions									
US	21	9 (42.9)	13.83 [2.73, NC]	23	4 (17.4)	NC [NC, NC]	0.000 [0.000, NC]	0.0461	0.1849
EU	76	7 (9.2)	NC [NC, NC]	69	2 (2.9)	NC [NC, NC]	0.894 [0.126, 6.348]	0.9138	
MOW	70	1 (1.4)	NC [NC, NC]	67	3 (4.5)	NC [NC, NC]	0.000 [0.000, NC]	0.0700	
Age Category									
< 65	29	2 (6.9)	NC [NC, NC]	28	3 (10.7)	NC [NC, NC]	0.316 [0.033, 3.035]	0.2916	0.1337
>= 65	138	15 (10.9)	NC [NC, NC]	131	6 (4.6)	NC [NC, NC]	0.153 [0.018, 1.272]	0.0454	
Sex									
Male	135	13 (9.6)	NC [NC, NC]	120	7 (5.8)	NC [NC, NC]	0.246 [0.051, 1.183]	0.0579	0.6666
Female	32	4 (12.5)	NC [NC, NC]	39	2 (5.1)	NC [NC, NC]	0.000 [0.000, NC]	0.1970	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.16.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Constipation (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	46 (27.5%)	13 (8.2%)	
Number of patients censored	121 (72.5%)	146 (91.8%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [14.98, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.855 [0.390, 1.873]
Log-rank test			
Two-sided unstratified log-rank p-value			0.6970

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.17.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Diarrhoea (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	57 (34.1%)	5 (3.1%)	
Number of patients censored	110 (65.9%)	154 (96.9%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [10.45, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			4.802 [1.832, 12.587]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0004

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.17.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Diarrhoea (PT)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	45 (32.6)	NC [8.21, NC]	129	5 (3.9)	NC [NC, NC]	3.689 [1.378, 9.881]	0.0053	0.9853
Eligible but Declined	29	12 (41.4)	NC [3.45, NC]	30	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0183	
Tumor Stage									
T2N0	31	10 (32.3)	NC [10.45, NC]	27	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0170	0.9998
T3/T4aN0	129	45 (34.9)	NC [7.82, NC]	125	5 (4.0)	NC [NC, NC]	3.191 [1.169, 8.711]	0.0167	
T1-4aN1	7	2 (28.6)	NC [0.36, NC]	7	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.1413	
Geographical Regions									
US	21	11 (52.4)	6.83 [0.72, NC]	23	1 (4.3)	NC [NC, NC]	6.991 [0.842, 58.078]	0.0354	0.5482
EU	76	33 (43.4)	8.21 [6.47, NC]	69	2 (2.9)	NC [NC, NC]	6.805 [1.546, 29.946]	0.0032	
MOW	70	13 (18.6)	NC [NC, NC]	67	2 (3.0)	NC [NC, NC]	1.926 [0.353, 10.514]	0.4410	
Age Category									
< 65	29	8 (27.6)	NC [7.23, NC]	28	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.1609	0.9865
>= 65	138	49 (35.5)	NC [8.21, NC]	131	5 (3.8)	NC [NC, NC]	4.412 [1.671, 11.651]	0.0010	
Sex									
Male	135	43 (31.9)	NC [11.17, NC]	120	4 (3.3)	NC [NC, NC]	4.190 [1.418, 12.382]	0.0048	0.5107
Female	32	14 (43.8)	8.77 [1.45, NC]	39	1 (2.6)	NC [NC, NC]	7.846 [0.945, 65.164]	0.0238	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.18.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Dry Mouth (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	18 (10.8%)	1 (0.6%)	
Number of patients censored	149 (89.2%)	158 (99.4%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			3.749 [0.419, 33.541]
Log-rank test			
Two-sided unstratified log-rank p-value			0.2043

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.19.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Nausea (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	43 (25.7%)	12 (7.5%)	
Number of patients censored	124 (74.3%)	147 (92.5%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			1.680 [0.827, 3.415]
Log-rank test			
Two-sided unstratified log-rank p-value			0.1470

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.20.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Vomiting (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	15 (9.0%)	6 (3.8%)	
Number of patients censored	152 (91.0%)	153 (96.2%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.625 [0.176, 2.214]
Log-rank test			
Two-sided unstratified log-rank p-value			0.4610

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.21.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - General Disorders and Administration Site Conditions (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	107 (64.1%)	22 (13.8%)	
Number of patients censored	60 (35.9%)	137 (86.2%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	3.35 [1.64, 4.93]	2.40 [1.54, NC]	
Difference in median			0.95
Cox proportional hazards model			
Unstratified HR, 95% CI			2.606 [1.592, 4.268]
Log-rank test			
Two-sided unstratified log-rank p-value			<.0001

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.21.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - General Disorders and Administration Site Conditions (SOC)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	85 (61.6)	3.71 [1.64, 5.85]	129	16 (12.4)	1.54 [1.54, NC]	2.947 [1.670, 5.202]	<.0001	0.5835
Eligible but Declined	29	22 (75.9)	2.14 [0.99, 4.93]	30	6 (20.0)	2.50 [NC, NC]	1.701 [0.618, 4.679]	0.2950	
Tumor Stage									
T2N0	31	25 (80.6)	1.02 [0.56, 1.64]	27	4 (14.8)	2.40 [NC, NC]	4.169 [1.393, 12.475]	0.0059	0.6180
T3/T4aN0	129	77 (59.7)	4.93 [2.69, 6.47]	125	18 (14.4)	1.54 [1.54, NC]	2.231 [1.278, 3.896]	0.0038	
T1-4aN1	7	5 (71.4)	4.14 [0.95, NC]	7	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.3173	
Geographical Regions									
US	21	18 (85.7)	1.05 [0.46, 3.29]	23	5 (21.7)	NC [NC, NC]	2.310 [0.788, 6.771]	0.1095	0.9607
EU	76	55 (72.4)	1.35 [0.92, 3.71]	69	11 (15.9)	1.54 [1.54, NC]	2.942 [1.482, 5.840]	0.0013	
MOW	70	34 (48.6)	7.85 [4.93, NC]	67	6 (9.0)	2.50 [NC, NC]	2.352 [0.906, 6.104]	0.0709	
Age Category									
< 65	29	20 (69.0)	4.14 [0.95, 6.64]	28	2 (7.1)	NC [NC, NC]	5.533 [1.212, 25.269]	0.0128	0.3235
>= 65	138	87 (63.0)	3.29 [1.41, 5.03]	131	20 (15.3)	2.40 [1.54, NC]	2.312 [1.368, 3.905]	0.0013	
Sex									
Male	135	88 (65.2)	3.71 [1.64, 5.03]	120	15 (12.5)	2.40 [1.54, NC]	2.659 [1.473, 4.800]	0.0008	0.3907
Female	32	19 (59.4)	2.35 [0.72, NC]	39	7 (17.9)	NC [NC, NC]	2.696 [1.097, 6.625]	0.0249	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.22.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Asthenia (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	29 (17.4%)	3 (1.9%)	
Number of patients censored	138 (82.6%)	156 (98.1%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			3.490 [0.974, 12.511]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0406

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.22.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Asthenia (PT)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	22 (15.9)	NC [NC, NC]	129	2 (1.6)	NC [NC, NC]	4.212 [0.910, 19.491]	0.0453	0.7043
Eligible but Declined	29	7 (24.1)	NC [14.98, NC]	30	1 (3.3)	NC [NC, NC]	2.046 [0.186, 22.569]	0.5503	
Tumor Stage									
T2N0	31	5 (16.1)	NC [NC, NC]	27	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.3507	0.9999
T3/T4aN0	129	22 (17.1)	NC [NC, NC]	125	3 (2.4)	NC [NC, NC]	3.217 [0.885, 11.690]	0.0602	
T1-4aN1	7	2 (28.6)	NC [1.18, NC]	7	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	
Geographical Regions									
US	21	2 (9.5)	NC [NC, NC]	23	2 (8.7)	NC [NC, NC]	0.515 [0.047, 5.682]	0.5809	0.1490
EU	76	16 (21.1)	NC [14.98, NC]	69	1 (1.4)	NC [NC, NC]	5.535 [0.667, 45.963]	0.0743	
MOW	70	11 (15.7)	NC [NC, NC]	67	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0505	
Age Category									
< 65	29	6 (20.7)	NC [NC, NC]	28	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.1609	0.9899
>= 65	138	23 (16.7)	NC [NC, NC]	131	3 (2.3)	NC [NC, NC]	2.822 [0.764, 10.425]	0.1035	
Sex									
Male	135	26 (19.3)	NC [NC, NC]	120	1 (0.8)	NC [NC, NC]	9.051 [1.159, 70.703]	0.0107	0.0621
Female	32	3 (9.4)	NC [8.05, NC]	39	2 (5.1)	NC [NC, NC]	0.588 [0.053, 6.488]	0.6648	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.23.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Fatigue (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	54 (32.3%)	7 (4.4%)	
Number of patients censored	113 (67.7%)	152 (95.6%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			4.718 [2.087, 10.667]
Log-rank test			
Two-sided unstratified log-rank p-value			<.0001

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.23.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Fatigue (PT)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	41 (29.7)	NC [NC, NC]	129	5 (3.9)	NC [NC, NC]	5.068 [1.946, 13.197]	0.0002	0.9220
Eligible but Declined	29	13 (44.8)	NC [1.08, NC]	30	2 (6.7)	NC [NC, NC]	3.890 [0.808, 18.735]	0.0678	
Tumor Stage									
T2N0	31	13 (41.9)	NC [1.08, NC]	27	2 (7.4)	NC [NC, NC]	4.159 [0.898, 19.264]	0.0473	0.9821
T3/T4aN0	129	38 (29.5)	NC [NC, NC]	125	5 (4.0)	NC [NC, NC]	4.653 [1.769, 12.240]	0.0006	
T1-4aN1	7	3 (42.9)	11.63 [0.95, NC]	7	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.3173	
Geographical Regions									
US	21	11 (52.4)	11.63 [0.72, NC]	23	2 (8.7)	NC [NC, NC]	3.969 [0.824, 19.127]	0.0623	0.4388
EU	76	35 (46.1)	10.87 [1.61, NC]	69	3 (4.3)	NC [NC, NC]	8.248 [2.482, 27.409]	<.0001	
MOW	70	8 (11.4)	NC [NC, NC]	67	2 (3.0)	NC [NC, NC]	0.928 [0.131, 6.586]	0.9401	
Age Category									
< 65	29	8 (27.6)	NC [NC, NC]	28	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0226	0.9837
>= 65	138	46 (33.3)	NC [11.63, NC]	131	7 (5.3)	NC [NC, NC]	3.960 [1.729, 9.066]	0.0004	
Sex									
Male	135	42 (31.1)	NC [NC, NC]	120	3 (2.5)	NC [NC, NC]	7.262 [2.180, 24.191]	0.0002	0.1510
Female	32	12 (37.5)	NC [0.99, NC]	39	4 (10.3)	NC [NC, NC]	3.052 [0.957, 9.738]	0.0473	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.24.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Oedema Peripheral (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	16 (9.6%)	3 (1.9%)	
Number of patients censored	151 (90.4%)	156 (98.1%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			1.869 [0.468, 7.474]
Log-rank test			
Two-sided unstratified log-rank p-value			0.3674

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.25.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Pyrexia (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	19 (11.4%)	4 (2.5%)	
Number of patients censored	148 (88.6%)	155 (97.5%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			2.130 [0.656, 6.915]
Log-rank test			
Two-sided unstratified log-rank p-value			0.1972

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.26.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Hepatobiliary Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	16 (9.6%)	1 (0.6%)	
Number of patients censored	151 (90.4%)	158 (99.4%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	2.43 [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			7.723 [0.967, 61.707]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0226

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.26.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Hepatobiliary Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	13 (9.4)	NC [NC, NC]	129	1 (0.8)	2.43 [NC, NC]	7.595 [0.950, 60.688]	0.0241	0.9925
Eligible but Declined	29	3 (10.3)	NC [NC, NC]	30	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	
Tumor Stage									
T2N0	31	4 (12.9)	NC [NC, NC]	27	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.1002	1.0000
T3/T4aN0	129	12 (9.3)	NC [NC, NC]	125	1 (0.8)	2.43 [NC, NC]	4.888 [0.572, 41.769]	0.1084	
T1-4aN1	7	0 (0.0)	NC [NC, NC]	7	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	
Geographical Regions									
US	21	1 (4.8)		23	0 (0.0)				
EU	76	9 (11.8)		69	0 (0.0)				
MOW	70	6 (8.6)		67	1 (1.5)				
Age Category									
< 65	29	3 (10.3)	NC [NC, NC]	28	1 (3.6)	2.43 [NC, NC]	1.120 [0.082, 15.333]	0.9325	0.9891
>= 65	138	13 (9.4)	NC [NC, NC]	131	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0098	
Sex									
Male	135	13 (9.6)	NC [NC, NC]	120	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0119	0.9896
Female	32	3 (9.4)	NC [NC, NC]	39	1 (2.6)	2.43 [NC, NC]	1.242 [0.083, 18.488]	0.8747	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.27.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Infections and Infestations (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	97 (58.1%)	48 (30.2%)	
Number of patients censored	70 (41.9%)	111 (69.8%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	4.70 [3.68, 7.39]	1.61 [1.15, 2.00]	
Difference in median			3.09
Cox proportional hazards model			
Unstratified HR, 95% CI			0.245 [0.147, 0.409]
Log-rank test			
Two-sided unstratified log-rank p-value			<.0001

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.27.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Infections and Infestations (SOC)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	83 (60.1)	4.21 [3.35, 6.93]	129	39 (30.2)	1.41 [1.15, 1.91]	0.260 [0.149, 0.454]	<.0001	0.2964
Eligible but Declined	29	14 (48.3)	8.11 [4.47, NC]	30	9 (30.0)	2.00 [2.00, NC]	0.180 [0.048, 0.672]	0.0077	
Tumor Stage									
T2N0	31	22 (71.0)	3.22 [2.40, 4.70]	27	7 (25.9)	1.15 [1.15, NC]	0.287 [0.082, 1.005]	0.0460	0.5002
T3/T4aN0	129	70 (54.3)	5.68 [3.91, 8.71]	125	38 (30.4)	1.84 [1.08, 2.69]	0.238 [0.131, 0.431]	<.0001	
T1-4aN1	7	5 (71.4)	4.21 [0.30, NC]	7	3 (42.9)	1.91 [0.39, NC]	0.318 [0.048, 2.087]	0.2145	
Geographical Regions									
US	21	14 (66.7)	3.68 [2.86, 8.11]	23	9 (39.1)	1.38 [0.99, NC]	0.108 [0.024, 0.487]	0.0021	0.8155
EU	76	43 (56.6)	5.22 [3.48, 8.28]	69	21 (30.4)	1.87 [1.15, 2.69]	0.316 [0.155, 0.643]	0.0011	
MOW	70	40 (57.1)	5.68 [3.35, 10.61]	67	18 (26.9)	1.84 [1.08, NC]	0.238 [0.097, 0.579]	0.0009	
Age Category									
< 65	29	16 (55.2)	8.71 [3.29, NC]	28	7 (25.0)	1.87 [1.87, NC]	0.227 [0.050, 1.025]	0.0425	0.7526
>= 65	138	81 (58.7)	4.47 [3.68, 6.77]	131	41 (31.3)	1.41 [1.15, 2.53]	0.254 [0.148, 0.435]	<.0001	
Sex									
Male	135	77 (57.0)	5.22 [3.75, 8.11]	120	33 (27.5)	1.61 [1.15, 2.69]	0.227 [0.124, 0.417]	<.0001	0.8736
Female	32	20 (62.5)	4.24 [2.30, 7.56]	39	15 (38.5)	1.84 [1.08, NC]	0.316 [0.119, 0.835]	0.0172	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.28.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Urinary Tract Infection (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	40 (24.0%)	20 (12.6%)	
Number of patients censored	127 (76.0%)	139 (87.4%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	1.84 [1.08, 2.76]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.155 [0.063, 0.380]
Log-rank test			
Two-sided unstratified log-rank p-value			<.0001

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.28.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Urinary Tract Infection (PT)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	33 (23.9)	NC [NC, NC]	129	17 (13.2)	1.84 [1.08, 2.76]	0.122 [0.045, 0.327]	<.0001	0.7921
Eligible but Declined	29	7 (24.1)	NC [NC, NC]	30	3 (10.0)	2.00 [NC, NC]	0.476 [0.071, 3.184]	0.4383	
Tumor Stage									
T2N0	31	9 (29.0)	NC [9.46, NC]	27	1 (3.7)	NC [NC, NC]	0.854 [0.053, 13.657]	0.9115	0.3810
T3/T4aN0	129	29 (22.5)	NC [NC, NC]	125	18 (14.4)	1.84 [1.08, 2.76]	0.154 [0.059, 0.401]	<.0001	
T1-4aN1	7	2 (28.6)	NC [1.18, NC]	7	1 (14.3)	2.00 [NC, NC]	0.154 [0.010, 2.472]	0.1284	
Geographical Regions									
US	21	8 (38.1)	NC [3.68, NC]	23	2 (8.7)	NC [NC, NC]	0.000 [0.000, NC]	0.1718	0.4907
EU	76	19 (25.0)	NC [10.78, NC]	69	10 (14.5)	2.69 [1.08, NC]	0.299 [0.097, 0.921]	0.0300	
MOW	70	13 (18.6)	NC [NC, NC]	67	8 (11.9)	1.84 [1.08, NC]	0.069 [0.018, 0.271]	0.0002	
Age Category									
< 65	29	7 (24.1)	NC [NC, NC]	28	3 (10.7)	2.00 [NC, NC]	0.148 [0.013, 1.652]	0.1094	0.9288
>= 65	138	33 (23.9)	NC [NC, NC]	131	17 (13.0)	1.84 [1.08, 2.76]	0.163 [0.063, 0.422]	0.0001	
Sex									
Male	135	32 (23.7)	NC [NC, NC]	120	14 (11.7)	2.69 [1.08, NC]	0.111 [0.037, 0.329]	<.0001	0.9042
Female	32	8 (25.0)	NC [NC, NC]	39	6 (15.4)	1.61 [1.08, NC]	0.342 [0.073, 1.600]	0.1626	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.29.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Injury, Poisoning and Procedural Complications (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	44 (26.3%)	29 (18.2%)	
Number of patients censored	123 (73.7%)	130 (81.8%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	1.87 [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.098 [0.032, 0.295]
Log-rank test			
Two-sided unstratified log-rank p-value			<.0001

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.29.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Injury, Poisoning and Procedural Complications (SOC)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	35 (25.4)	NC [NC, NC]	129	22 (17.1)	1.87 [NC, NC]	0.127 [0.041, 0.392]	<.0001	0.7045
Eligible but Declined	29	9 (31.0)	NC [4.01, NC]	30	7 (23.3)	NC [NC, NC]	0.000 [0.000, NC]	0.0060	
Tumor Stage									
T2N0	31	10 (32.3)	NC [3.19, NC]	27	2 (7.4)	NC [NC, NC]	0.000 [0.000, NC]	0.1261	0.1798
T3/T4aN0	129	31 (24.0)	NC [NC, NC]	125	24 (19.2)	1.87 [NC, NC]	0.084 [0.023, 0.303]	<.0001	
T1-4aN1	7	3 (42.9)	NC [0.07, NC]	7	3 (42.9)	NC [0.03, NC]	0.294 [0.030, 2.825]	0.2504	
Geographical Regions									
US	21	14 (66.7)	3.81 [3.06, 6.05]	23	8 (34.8)	NC [0.07, NC]	0.220 [0.047, 1.038]	0.0380	0.4884
EU	76	15 (19.7)	NC [NC, NC]	69	11 (15.9)	NC [NC, NC]	0.000 [0.000, NC]	0.0003	
MOW	70	15 (21.4)	NC [NC, NC]	67	10 (14.9)	1.87 [NC, NC]	0.115 [0.021, 0.636]	0.0044	
Age Category									
< 65	29	10 (34.5)	NC [4.34, NC]	28	3 (10.7)	NC [NC, NC]	0.000 [0.000, NC]	0.0725	0.2678
>= 65	138	34 (24.6)	NC [NC, NC]	131	26 (19.8)	1.87 [NC, NC]	0.109 [0.036, 0.327]	<.0001	
Sex									
Male	135	35 (25.9)	NC [NC, NC]	120	23 (19.2)	NC [NC, NC]	0.035 [0.005, 0.259]	<.0001	0.3374
Female	32	9 (28.1)	NC [2.89, NC]	39	6 (15.4)	1.87 [NC, NC]	0.401 [0.086, 1.871]	0.2302	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.30.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Procedural Pain (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	9 (5.4%)	12 (7.5%)	
Number of patients censored	158 (94.6%)	147 (92.5%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.000 [0.000, NC]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0003

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.30.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Procedural Pain (PT)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	7 (5.1)	NC [NC, NC]	129	7 (5.4)	NC [NC, NC]	0.000 [0.000, NC]	0.0056	0.4020
Eligible but Declined	29	2 (6.9)	NC [NC, NC]	30	5 (16.7)	NC [NC, NC]	0.000 [0.000, NC]	0.0227	
Tumor Stage									
T2N0	31	4 (12.9)	NC [NC, NC]	27	1 (3.7)	NC [NC, NC]	0.000 [0.000, NC]	0.2839	0.2214
T3/T4aN0	129	5 (3.9)	NC [NC, NC]	125	11 (8.8)	NC [NC, NC]	0.000 [0.000, NC]	0.0006	
T1-4aN1	7	0 (0.0)	NC [NC, NC]	7	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	
Geographical Regions									
US	21	2 (9.5)		23	4 (17.4)				
EU	76	3 (3.9)		69	6 (8.7)				
MOW	70	4 (5.7)		67	2 (3.0)				
Age Category									
< 65	29	3 (10.3)	NC [NC, NC]	28	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	0.9966
>= 65	138	6 (4.3)	NC [NC, NC]	131	12 (9.2)	NC [NC, NC]	0.000 [0.000, NC]	0.0003	
Sex									
Male	135	7 (5.2)	NC [NC, NC]	120	9 (7.5)	NC [NC, NC]	0.000 [0.000, NC]	0.0012	0.8724
Female	32	2 (6.3)	NC [NC, NC]	39	3 (7.7)	NC [NC, NC]	0.000 [0.000, NC]	0.1117	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.31.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Investigations (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	86 (51.5%)	15 (9.4%)	
Number of patients censored	81 (48.5%)	144 (90.6%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	6.14 [3.98, 13.24]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			2.365 [1.295, 4.319]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0040

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.31.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Investigations (SOC)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	64 (46.4)	8.21 [4.01, NC]	129	11 (8.5)	NC [NC, NC]	2.858 [1.440, 5.670]	0.0017	0.8870
Eligible but Declined	29	22 (75.9)	3.38 [1.91, 5.62]	30	4 (13.3)	NC [NC, NC]	1.005 [0.251, 4.020]	0.9941	
Tumor Stage									
T2N0	31	14 (45.2)	NC [1.18, NC]	27	2 (7.4)	NC [NC, NC]	3.401 [0.706, 16.379]	0.1051	0.9544
T3/T4aN0	129	66 (51.2)	6.28 [3.94, 14.06]	125	12 (9.6)	NC [NC, NC]	2.201 [1.115, 4.344]	0.0200	
T1-4aN1	7	6 (85.7)	2.63 [0.26, NC]	7	1 (14.3)	NC [0.95, NC]	2.363 [0.213, 26.186]	0.4703	
Geographical Regions									
US	21	16 (76.2)	2.76 [0.72, 4.27]	23	3 (13.0)	NC [NC, NC]	3.384 [0.914, 12.525]	0.0560	0.6713
EU	76	41 (53.9)	4.86 [1.61, 17.28]	69	6 (8.7)	NC [NC, NC]	2.688 [1.059, 6.819]	0.0305	
MOW	70	29 (41.4)	10.68 [6.14, NC]	67	6 (9.0)	NC [NC, NC]	1.639 [0.596, 4.509]	0.3351	
Age Category									
< 65	29	13 (44.8)	17.28 [3.35, NC]	28	2 (7.1)	NC [NC, NC]	0.956 [0.135, 6.787]	0.9641	0.8774
>= 65	138	73 (52.9)	5.95 [3.94, 8.21]	131	13 (9.9)	NC [NC, NC]	2.597 [1.370, 4.922]	0.0025	
Sex									
Male	135	69 (51.1)	6.28 [3.98, 14.06]	120	11 (9.2)	NC [NC, NC]	2.290 [1.136, 4.617]	0.0174	0.9398
Female	32	17 (53.1)	3.09 [1.38, NC]	39	4 (10.3)	NC [NC, NC]	2.711 [0.835, 8.806]	0.0881	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.32.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Alanine Aminotransferase Increased (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	32 (19.2%)	2 (1.3%)	
Number of patients censored	135 (80.8%)	157 (98.7%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			9.434 [2.197, 40.505]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0002

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.32.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Alanine Aminotransferase Increased (PT)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	25 (18.1)	NC [NC, NC]	129	1 (0.8)	NC [NC, NC]	15.491 [2.055, 116.76]	0.0004	0.4230
Eligible but Declined	29	7 (24.1)	NC [NC, NC]	30	1 (3.3)	NC [NC, NC]	3.277 [0.341, 31.513]	0.2761	
Tumor Stage									
T2N0	31	6 (19.4)	NC [NC, NC]	27	1 (3.7)	NC [NC, NC]	3.731 [0.417, 33.396]	0.2061	0.6248
T3/T4aN0	129	24 (18.6)	NC [NC, NC]	125	1 (0.8)	NC [NC, NC]	13.986 [1.839, 106.34]	0.0008	
T1-4aN1	7	2 (28.6)	NC [0.72, NC]	7	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.3173	
Geographical Regions									
US	21	8 (38.1)	NC [2.14, NC]	23	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0162	0.9383
EU	76	15 (19.7)	NC [NC, NC]	69	1 (1.4)	NC [NC, NC]	7.650 [0.957, 61.168]	0.0235	
MOW	70	9 (12.9)	NC [NC, NC]	67	1 (1.5)	NC [NC, NC]	5.858 [0.705, 48.636]	0.0630	
Age Category									
< 65	29	3 (10.3)	NC [NC, NC]	28	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.3258	0.9900
>= 65	138	29 (21.0)	NC [NC, NC]	131	2 (1.5)	NC [NC, NC]	8.959 [2.079, 38.615]	0.0004	
Sex									
Male	135	21 (15.6)	NC [NC, NC]	120	2 (1.7)	NC [NC, NC]	5.524 [1.237, 24.675]	0.0117	0.9880
Female	32	11 (34.4)	NC [1.41, NC]	39	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0027	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.33.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Aspartate Aminotransferase Increased (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	40 (24.0%)	0 (0.0%)	
Number of patients censored	127 (76.0%)	159 (100.0%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			NC [NC, NC]
Log-rank test			
Two-sided unstratified log-rank p-value			<.0001

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.33.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Aspartate Aminotransferase Increased (PT)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	31 (22.5)	NC [NC, NC]	129	0 (0.0)	NC [NC, NC]	NC [NC, NC]	<.0001	0.9999
Eligible but Declined	29	9 (31.0)	NC [9.43, NC]	30	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0729	
Tumor Stage									
T2N0	31	9 (29.0)	NC [9.59, NC]	27	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0556	1.0000
T3/T4aN0	129	28 (21.7)	NC [NC, NC]	125	0 (0.0)	NC [NC, NC]	NC [NC, NC]	<.0001	
T1-4aN1	7	3 (42.9)	NC [0.72, NC]	7	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.3173	
Geographical Regions									
US	21	10 (47.6)	14.06 [0.72, NC]	23	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0076	1.0000
EU	76	21 (27.6)	NC [NC, NC]	69	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0011	
MOW	70	9 (12.9)	NC [NC, NC]	67	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0276	
Age Category									
< 65	29	5 (17.2)	NC [NC, NC]	28	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.3258	0.9999
>= 65	138	35 (25.4)	NC [NC, NC]	131	0 (0.0)	NC [NC, NC]	NC [NC, NC]	<.0001	
Sex									
Male	135	29 (21.5)	NC [NC, NC]	120	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0003	0.9997
Female	32	11 (34.4)	NC [1.41, NC]	39	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0012	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.34.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Blood Creatinine Increased (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	19 (11.4%)	6 (3.8%)	
Number of patients censored	148 (88.6%)	153 (96.2%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			1.427 [0.508, 4.008]
Log-rank test			
Two-sided unstratified log-rank p-value			0.5014

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.35.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Weight Decreased (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	33 (19.8%)	5 (3.1%)	
Number of patients censored	134 (80.2%)	154 (96.9%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.373 [0.072, 1.924]
Log-rank test			
Two-sided unstratified log-rank p-value			0.2201

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.36.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Metabolism and Nutrition Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	90 (53.9%)	19 (11.9%)	
Number of patients censored	77 (46.1%)	140 (88.1%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	4.47 [3.65, 7.69]	2.56 [NC, NC]	
Difference in median			1.91
Cox proportional hazards model			
Unstratified HR, 95% CI			2.182 [1.267, 3.756]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0040

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.36.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Metabolism and Nutrition Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	70 (50.7)	4.63 [3.94, 15.34]	129	16 (12.4)	2.56 [NC, NC]	2.045 [1.127, 3.712]	0.0165	0.4017
Eligible but Declined	29	20 (69.0)	2.79 [1.22, 7.75]	30	3 (10.0)	NC [NC, NC]	2.920 [0.774, 11.016]	0.0975	
Tumor Stage									
T2N0	31	16 (51.6)	4.24 [2.76, NC]	27	2 (7.4)	NC [NC, NC]	2.293 [0.445, 11.825]	0.3092	0.7868
T3/T4aN0	129	69 (53.5)	4.63 [2.79, 10.18]	125	16 (12.8)	2.56 [NC, NC]	2.186 [1.208, 3.956]	0.0083	
T1-4aN1	7	5 (71.4)	3.81 [0.03, NC]	7	1 (14.3)	NC [0.16, NC]	2.107 [0.191, 23.269]	0.5337	
Geographical Regions									
US	21	13 (61.9)	2.89 [0.26, NC]	23	7 (30.4)	NC [0.99, NC]	1.737 [0.661, 4.569]	0.2671	0.2499
EU	76	39 (51.3)	5.42 [4.24, NC]	69	6 (8.7)	NC [NC, NC]	3.283 [1.318, 8.180]	0.0068	
MOW	70	38 (54.3)	4.47 [2.76, 15.34]	67	6 (9.0)	2.56 [NC, NC]	1.810 [0.676, 4.845]	0.2312	
Age Category									
< 65	29	15 (51.7)	10.18 [4.30, NC]	28	5 (17.9)	2.56 [NC, NC]	0.674 [0.177, 2.566]	0.5614	0.1540
>= 65	138	75 (54.3)	4.24 [2.76, 6.24]	131	14 (10.7)	NC [NC, NC]	2.738 [1.484, 5.055]	0.0008	
Sex									
Male	135	74 (54.8)	4.40 [2.89, 10.18]	120	16 (13.3)	2.56 [NC, NC]	1.954 [1.077, 3.546]	0.0253	0.4570
Female	32	16 (50.0)	7.16 [2.69, NC]	39	3 (7.7)	NC [NC, NC]	3.381 [0.897, 12.745]	0.0560	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.37.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Decreased Appetite (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	47 (28.1%)	3 (1.9%)	
Number of patients censored	120 (71.9%)	156 (98.1%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [15.67, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			5.537 [1.623, 18.892]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0021

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.37.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Decreased Appetite (PT)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	37 (26.8)	NC [NC, NC]	129	3 (2.3)	NC [NC, NC]	4.468 [1.284, 15.547]	0.0099	0.9881
Eligible but Declined	29	10 (34.5)	15.67 [7.59, NC]	30	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0729	
Tumor Stage									
T2N0	31	7 (22.6)	NC [11.76, NC]	27	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.1833	0.9999
T3/T4aN0	129	39 (30.2)	NC [15.67, NC]	125	3 (2.4)	NC [NC, NC]	4.965 [1.438, 17.150]	0.0049	
T1-4aN1	7	1 (14.3)	NC [6.24, NC]	7	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	
Geographical Regions									
US	21	5 (23.8)	NC [4.96, NC]	23	2 (8.7)	NC [NC, NC]	1.573 [0.263, 9.416]	0.6227	0.3734
EU	76	24 (31.6)	15.67 [11.27, NC]	69	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0033	
MOW	70	18 (25.7)	NC [NC, NC]	67	1 (1.5)	NC [NC, NC]	4.766 [0.557, 40.789]	0.1153	
Age Category									
< 65	29	7 (24.1)	NC [NC, NC]	28	1 (3.6)	NC [NC, NC]	3.001 [0.312, 28.858]	0.3171	0.3342
>= 65	138	40 (29.0)	NC [15.67, NC]	131	2 (1.5)	NC [NC, NC]	6.794 [1.544, 29.895]	0.0033	
Sex									
Male	135	38 (28.1)	NC [15.67, NC]	120	2 (1.7)	NC [NC, NC]	5.439 [1.218, 24.296]	0.0126	0.7686
Female	32	9 (28.1)	NC [7.59, NC]	39	1 (2.6)	NC [NC, NC]	6.344 [0.741, 54.300]	0.0528	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.38.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Hyperglycaemia (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	21 (12.6%)	1 (0.6%)	
Number of patients censored	146 (87.4%)	158 (99.4%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			13.769 [1.811, 104.68]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0009

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.38.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Hyperglycaemia (PT)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	17 (12.3)	NC [NC, NC]	129	1 (0.8)	NC [NC, NC]	10.539 [1.361, 81.630]	0.0049	0.9908
Eligible but Declined	29	4 (13.8)	NC [NC, NC]	30	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0729	
Tumor Stage									
T2N0	31	4 (12.9)	NC [NC, NC]	27	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.1001	0.9999
T3/T4aN0	129	16 (12.4)	NC [NC, NC]	125	1 (0.8)	NC [NC, NC]	10.952 [1.414, 84.824]	0.0040	
T1-4aN1	7	1 (14.3)	NC [1.41, NC]	7	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	
Geographical Regions									
US	21	4 (19.0)	NC [NC, NC]	23	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.1343	0.9999
EU	76	7 (9.2)	NC [NC, NC]	69	1 (1.4)	NC [NC, NC]	6.668 [0.820, 54.201]	0.0401	
MOW	70	10 (14.3)	NC [15.34, NC]	67	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0286	
Age Category									
< 65	29	3 (10.3)	NC [15.34, NC]	28	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.3258	0.9916
>= 65	138	18 (13.0)	NC [NC, NC]	131	1 (0.8)	NC [NC, NC]	12.807 [1.676, 97.888]	0.0015	
Sex									
Male	135	20 (14.8)	NC [NC, NC]	120	1 (0.8)	NC [NC, NC]	12.075 [1.580, 92.293]	0.0021	0.9913
Female	32	1 (3.1)	NC [NC, NC]	39	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.2822	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.39.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Hyperkalaemia (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	10 (6.0%)	2 (1.3%)	
Number of patients censored	157 (94.0%)	157 (98.7%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	2.56 [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.000 [0.000, NC]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0028

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.39.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Hyperkalaemia (PT)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	9 (6.5)	NC [NC, NC]	129	2 (1.6)	2.56 [NC, NC]	0.000 [0.000, NC]	0.0028	0.9992
Eligible but Declined	29	1 (3.4)	NC [NC, NC]	30	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	
Tumor Stage									
T2N0	31	2 (6.5)		27	1 (3.7)				
T3/T4aN0	129	8 (6.2)		125	1 (0.8)				
T1-4aN1	7	0 (0.0)		7	0 (0.0)				
Geographical Regions									
US	21	0 (0.0)		23	0 (0.0)				
EU	76	6 (7.9)		69	1 (1.4)				
MOW	70	4 (5.7)		67	1 (1.5)				
Age Category									
< 65	29	2 (6.9)		28	2 (7.1)				
>= 65	138	8 (5.8)		131	0 (0.0)				
Sex									
Male	135	7 (5.2)		120	2 (1.7)				
Female	32	3 (9.4)		39	0 (0.0)				

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.40.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Hypokalaemia (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	16 (9.6%)	4 (2.5%)	
Number of patients censored	151 (90.4%)	155 (97.5%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.935 [0.234, 3.739]
Log-rank test			
Two-sided unstratified log-rank p-value			0.9254

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.41.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Hyponatraemia (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	12 (7.2%)	0 (0.0%)	
Number of patients censored	155 (92.8%)	159 (100.0%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			NC [NC, NC]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0509

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.42.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Musculoskeletal and Connective Tissue Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	39 (23.4%)	4 (2.5%)	
Number of patients censored	128 (76.6%)	155 (97.5%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			2.624 [0.836, 8.240]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0857

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.43.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Arthralgia (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	10 (6.0%)	1 (0.6%)	
Number of patients censored	157 (94.0%)	158 (99.4%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			1.915 [0.174, 21.124]
Log-rank test			
Two-sided unstratified log-rank p-value			0.5899

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.44.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Neoplasms Benign, Malignant and Unspecified (Incl Cysts and Polyps) (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	23 (13.8%)	15 (9.4%)	
Number of patients censored	144 (86.2%)	144 (90.6%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.180 [0.052, 0.622]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0025

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.44.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Neoplasms Benign, Malignant and Unspecified (Incl Cysts and Polyps) (SOC)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	17 (12.3)	NC [NC, NC]	129	13 (10.1)	NC [NC, NC]	0.136 [0.031, 0.601]	0.0022	0.2951
Eligible but Declined	29	6 (20.7)	NC [NC, NC]	30	2 (6.7)	NC [NC, NC]	0.500 [0.045, 5.513]	0.5678	
Tumor Stage									
T2N0	31	4 (12.9)	NC [NC, NC]	27	1 (3.7)	NC [NC, NC]	0.000 [0.000, NC]	0.2839	0.7350
T3/T4aN0	129	19 (14.7)	NC [NC, NC]	125	13 (10.4)	NC [NC, NC]	0.210 [0.060, 0.736]	0.0078	
T1-4aN1	7	0 (0.0)	NC [NC, NC]	7	1 (14.3)	NC [0.03, NC]	NC [NC, NC]	0.3173	
Geographical Regions									
US	21	2 (9.5)	NC [NC, NC]	23	4 (17.4)	NC [NC, NC]	0.249 [0.028, 2.230]	0.1863	0.2944
EU	76	10 (13.2)	NC [NC, NC]	69	7 (10.1)	NC [NC, NC]	0.123 [0.015, 1.000]	0.0202	
MOW	70	11 (15.7)	NC [NC, NC]	67	4 (6.0)	NC [NC, NC]	0.231 [0.026, 2.070]	0.1552	
Age Category									
< 65	29	3 (10.3)	NC [NC, NC]	28	3 (10.7)	NC [NC, NC]	0.000 [0.000, NC]	0.0726	0.4531
>= 65	138	20 (14.5)	NC [NC, NC]	131	12 (9.2)	NC [NC, NC]	0.224 [0.063, 0.795]	0.0121	
Sex									
Male	135	22 (16.3)	NC [NC, NC]	120	15 (12.5)	NC [NC, NC]	0.165 [0.048, 0.571]	0.0013	0.9887
Female	32	1 (3.1)	NC [12.19, NC]	39	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.45.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Prostate Cancer (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	19 (11.4%)	15 (9.4%)	
Number of patients censored	148 (88.6%)	144 (90.6%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.060 [0.008, 0.457]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0002

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.45.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Prostate Cancer (PT)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	15 (10.9)	NC [NC, NC]	129	13 (10.1)	NC [NC, NC]	0.068 [0.009, 0.520]	0.0006	0.4969
Eligible but Declined	29	4 (13.8)	NC [NC, NC]	30	2 (6.7)	NC [NC, NC]	0.000 [0.000, NC]	0.1607	
Tumor Stage									
T2N0	31	2 (6.5)	NC [NC, NC]	27	1 (3.7)	NC [NC, NC]	0.000 [0.000, NC]	0.2839	0.9662
T3/T4aN0	129	17 (13.2)	NC [NC, NC]	125	13 (10.4)	NC [NC, NC]	0.070 [0.009, 0.539]	0.0008	
T1-4aN1	7	0 (0.0)	NC [NC, NC]	7	1 (14.3)	NC [0.03, NC]	NC [NC, NC]	0.3173	
Geographical Regions									
US	21	2 (9.5)	NC [NC, NC]	23	4 (17.4)	NC [NC, NC]	0.000 [0.000, NC]	0.0475	0.3570
EU	76	8 (10.5)	NC [NC, NC]	69	7 (10.1)	NC [NC, NC]	0.123 [0.015, 1.000]	0.0202	
MOW	70	9 (12.9)	NC [NC, NC]	67	4 (6.0)	NC [NC, NC]	0.000 [0.000, NC]	0.0387	
Age Category									
< 65	29	3 (10.3)	NC [NC, NC]	28	3 (10.7)	NC [NC, NC]	0.000 [0.000, NC]	0.0726	0.6513
>= 65	138	16 (11.6)	NC [NC, NC]	131	12 (9.2)	NC [NC, NC]	0.075 [0.010, 0.579]	0.0013	
Sex									
Male	135	19 (14.1)	NC [NC, NC]	120	15 (12.5)	NC [NC, NC]	0.055 [0.007, 0.420]	0.0001	0.9996
Female	32	0 (0.0)	NC [NC, NC]	39	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.46.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Nervous System Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	98 (58.7%)	4 (2.5%)	
Number of patients censored	69 (41.3%)	155 (97.5%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	4.37 [1.91, 6.67]	1.25 [NC, NC]	
Difference in median			3.12
Cox proportional hazards model			
Unstratified HR, 95% CI			13.733 [4.959, 38.032]
Log-rank test			
Two-sided unstratified log-rank p-value			<.0001

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.46.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Nervous System Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	80 (58.0)	4.63 [1.84, 6.93]	129	4 (3.1)	1.25 [NC, NC]	10.669 [3.816, 29.823]	<.0001	0.9822
Eligible but Declined	29	18 (62.1)	2.86 [0.76, 5.26]	30	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0004	
Tumor Stage									
T2N0	31	20 (64.5)	2.73 [1.35, 7.10]	27	1 (3.7)	NC [NC, NC]	8.648 [1.095, 68.319]	0.0137	0.9635
T3/T4aN0	129	74 (57.4)	4.70 [2.10, 6.77]	125	3 (2.4)	1.25 [NC, NC]	13.742 [4.237, 44.573]	<.0001	
T1-4aN1	7	4 (57.1)	0.76 [0.46, NC]	7	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0221	
Geographical Regions									
US	21	19 (90.5)	0.69 [0.36, 1.31]	23	0 (0.0)	NC [NC, NC]	NC [NC, NC]	<.0001	0.9350
EU	76	47 (61.8)	2.86 [1.31, 5.55]	69	3 (4.3)	1.25 [NC, NC]	9.451 [2.859, 31.245]	<.0001	
MOW	70	32 (45.7)	7.10 [5.26, NC]	67	1 (1.5)	NC [NC, NC]	11.894 [1.546, 91.470]	0.0024	
Age Category									
< 65	29	17 (58.6)	5.55 [0.76, NC]	28	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0014	0.9832
>= 65	138	81 (58.7)	3.48 [1.84, 6.67]	131	4 (3.1)	1.25 [NC, NC]	11.147 [3.992, 31.126]	<.0001	
Sex									
Male	135	79 (58.5)	4.63 [1.97, 6.77]	120	3 (2.5)	1.25 [NC, NC]	12.831 [3.960, 41.573]	<.0001	0.9484
Female	32	19 (59.4)	1.68 [0.82, NC]	39	1 (2.6)	NC [NC, NC]	17.552 [2.281, 135.07]	0.0002	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.47.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Dizziness (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	12 (7.2%)	0 (0.0%)	
Number of patients censored	155 (92.8%)	159 (100.0%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			NC [NC, NC]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0518

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.48.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Dysgeusia (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	47 (28.1%)	0 (0.0%)	
Number of patients censored	120 (71.9%)	159 (100.0%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			NC [NC, NC]
Log-rank test			
Two-sided unstratified log-rank p-value			<.0001

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.48.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Dysgeusia (PT)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	40 (29.0)	NC [NC, NC]	129	0 (0.0)	NC [NC, NC]	NC [NC, NC]	<.0001	0.9999
Eligible but Declined	29	7 (24.1)	NC [NC, NC]	30	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0184	
Tumor Stage									
T2N0	31	12 (38.7)	NC [1.97, NC]	27	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0170	1.0000
T3/T4aN0	129	33 (25.6)	NC [NC, NC]	125	0 (0.0)	NC [NC, NC]	NC [NC, NC]	<.0001	
T1-4aN1	7	2 (28.6)	NC [0.56, NC]	7	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.1413	
Geographical Regions									
US	21	11 (52.4)	3.29 [1.15, NC]	23	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0150	1.0000
EU	76	22 (28.9)	NC [NC, NC]	69	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0002	
MOW	70	14 (20.0)	NC [NC, NC]	67	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0053	
Age Category									
< 65	29	10 (34.5)	NC [4.70, NC]	28	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0030	0.9999
>= 65	138	37 (26.8)	NC [NC, NC]	131	0 (0.0)	NC [NC, NC]	NC [NC, NC]	<.0001	
Sex									
Male	135	38 (28.1)	NC [NC, NC]	120	0 (0.0)	NC [NC, NC]	NC [NC, NC]	<.0001	1.0000
Female	32	9 (28.1)	NC [NC, NC]	39	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0562	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.49.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Neuropathy Peripheral (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	17 (10.2%)	0 (0.0%)	
Number of patients censored	150 (89.8%)	159 (100.0%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			NC [NC, NC]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0931

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.50.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Paraesthesia (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	11 (6.6%)	0 (0.0%)	
Number of patients censored	156 (93.4%)	159 (100.0%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			NC [NC, NC]
Log-rank test			
Two-sided unstratified log-rank p-value			0.3292

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.51.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Peripheral Sensory Neuropathy (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	23 (13.8%)	0 (0.0%)	
Number of patients censored	144 (86.2%)	159 (100.0%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			NC [NC, NC]
Log-rank test			
Two-sided unstratified log-rank p-value			0.3292

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.52.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Taste Disorder (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	11 (6.6%)	0 (0.0%)	
Number of patients censored	156 (93.4%)	159 (100.0%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			NC [NC, NC]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0094

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.52.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Taste Disorder (PT)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	10 (7.2)	NC [NC, NC]	129	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0173	0.9999
Eligible but Declined	29	1 (3.4)	NC [NC, NC]	30	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.3091	
Tumor Stage									
T2N0	31	2 (6.5)		27	0 (0.0)				
T3/T4aN0	129	8 (6.2)		125	0 (0.0)				
T1-4aN1	7	1 (14.3)		7	0 (0.0)				
Geographical Regions									
US	21	2 (9.5)		23	0 (0.0)				
EU	76	4 (5.3)		69	0 (0.0)				
MOW	70	5 (7.1)		67	0 (0.0)				
Age Category									
< 65	29	0 (0.0)	NC [NC, NC]	28	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	0.9979
>= 65	138	11 (8.0)	NC [NC, NC]	131	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0094	
Sex									
Male	135	8 (5.9)		120	0 (0.0)				
Female	32	3 (9.4)		39	0 (0.0)				

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.53.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Psychiatric Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	28 (16.8%)	10 (6.3%)	
Number of patients censored	139 (83.2%)	149 (93.7%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	1.81 [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.653 [0.250, 1.709]
Log-rank test			
Two-sided unstratified log-rank p-value			0.3827

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.54.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Insomnia (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	18 (10.8%)	7 (4.4%)	
Number of patients censored	149 (89.2%)	152 (95.6%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.793 [0.267, 2.361]
Log-rank test			
Two-sided unstratified log-rank p-value			0.6767

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.55.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Renal and Urinary Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	44 (26.3%)	14 (8.8%)	
Number of patients censored	123 (73.7%)	145 (91.2%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	1.41 [1.41, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.712 [0.322, 1.573]
Log-rank test			
Two-sided unstratified log-rank p-value			0.3993

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.56.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Acute Kidney Injury (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	11 (6.6%)	4 (2.5%)	
Number of patients censored	156 (93.4%)	155 (97.5%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	1.41 [1.41, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.015 [0.001, 0.154]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0042

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.56.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Acute Kidney Injury (PT)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	9 (6.5)	NC [NC, NC]	129	4 (3.1)	1.41 [1.41, NC]	0.010 [0.001, 0.155]	0.0038	0.9927
Eligible but Declined	29	2 (6.9)	NC [NC, NC]	30	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	
Tumor Stage									
T2N0	31	1 (3.2)	NC [NC, NC]	27	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	1.0000
T3/T4aN0	129	8 (6.2)	NC [NC, NC]	125	4 (3.2)	1.41 [1.41, NC]	0.019 [0.002, 0.192]	0.0046	
T1-4aN1	7	2 (28.6)	NC [6.77, NC]	7	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	
Geographical Regions									
US	21	1 (4.8)		23	2 (8.7)				
EU	76	4 (5.3)		69	0 (0.0)				
MOW	70	6 (8.6)		67	2 (3.0)				
Age Category									
< 65	29	3 (10.3)	NC [NC, NC]	28	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	0.9926
>= 65	138	8 (5.8)	NC [NC, NC]	131	4 (3.1)	1.41 [1.41, NC]	0.018 [0.002, 0.182]	0.0043	
Sex									
Male	135	7 (5.2)		120	2 (1.7)				
Female	32	4 (12.5)		39	2 (5.1)				

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.57.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Haematuria (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	11 (6.6%)	1 (0.6%)	
Number of patients censored	156 (93.4%)	158 (99.4%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			5.716 [0.688, 47.458]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0676

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.58.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Reproductive System and Breast Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	17 (10.2%)	4 (2.5%)	
Number of patients censored	150 (89.8%)	155 (97.5%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.000 [0.000, NC]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0390

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.58.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Reproductive System and Breast Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	14 (10.1)	NC [NC, NC]	129	1 (0.8)	NC [NC, NC]	0.000 [0.000, NC]	0.3010	0.0423
Eligible but Declined	29	3 (10.3)	NC [NC, NC]	30	3 (10.0)	NC [NC, NC]	0.000 [0.000, NC]	0.0832	
Tumor Stage									
T2N0	31	3 (9.7)	NC [NC, NC]	27	2 (7.4)	NC [NC, NC]	0.000 [0.000, NC]	0.1261	0.4541
T3/T4aN0	129	12 (9.3)	NC [NC, NC]	125	2 (1.6)	NC [NC, NC]	0.000 [0.000, NC]	0.1492	
T1-4aN1	7	2 (28.6)	13.90 [4.44, NC]	7	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	
Geographical Regions									
US	21	5 (23.8)	NC [3.98, NC]	23	1 (4.3)	NC [NC, NC]	0.000 [0.000, NC]	0.3286	0.9084
EU	76	8 (10.5)	NC [NC, NC]	69	2 (2.9)	NC [NC, NC]	0.000 [0.000, NC]	0.1363	
MOW	70	4 (5.7)	NC [NC, NC]	67	1 (1.5)	NC [NC, NC]	0.000 [0.000, NC]	0.3067	
Age Category									
< 65	29	3 (10.3)	NC [NC, NC]	28	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	0.9955
>= 65	138	14 (10.1)	NC [NC, NC]	131	4 (3.1)	NC [NC, NC]	0.000 [0.000, NC]	0.0384	
Sex									
Male	135	12 (8.9)	NC [NC, NC]	120	3 (2.5)	NC [NC, NC]	0.000 [0.000, NC]	0.0651	0.6057
Female	32	5 (15.6)	NC [NC, NC]	39	1 (2.6)	NC [NC, NC]	0.000 [0.000, NC]	0.3588	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.59.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Respiratory, Thoracic and Mediastinal Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	45 (26.9%)	12 (7.5%)	
Number of patients censored	122 (73.1%)	147 (92.5%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	1.38 [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			1.419 [0.684, 2.944]
Log-rank test			
Two-sided unstratified log-rank p-value			0.3455

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.60.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Skin and Subcutaneous Tissue Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	143 (85.6%)	4 (2.5%)	
Number of patients censored	24 (14.4%)	155 (97.5%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	0.49 [0.36, 0.56]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			43.612 [16.064, 118.40]
Log-rank test			
Two-sided unstratified log-rank p-value			<.0001

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.60.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Skin and Subcutaneous Tissue Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	117 (84.8)	0.49 [0.36, 0.69]	129	1 (0.8)	NC [NC, NC]	142.00 [19.775, 1019.6]	<.0001	0.0360
Eligible but Declined	29	26 (89.7)	0.46 [0.30, 0.62]	30	3 (10.0)	NC [NC, NC]	10.538 [3.115, 35.645]	<.0001	
Tumor Stage									
T2N0	31	28 (90.3)	0.30 [0.26, 0.72]	27	0 (0.0)	NC [NC, NC]	NC [NC, NC]	<.0001	0.9995
T3/T4aN0	129	108 (83.7)	0.49 [0.36, 0.66]	125	4 (3.2)	NC [NC, NC]	33.754 [12.366, 92.133]	<.0001	
T1-4aN1	7	7 (100.0)	0.69 [0.10, 1.31]	7	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0221	
Geographical Regions									
US	21	20 (95.2)	0.46 [0.20, 0.76]	23	0 (0.0)	NC [NC, NC]	NC [NC, NC]	<.0001	0.5607
EU	76	67 (88.2)	0.56 [0.36, 0.79]	69	1 (1.4)	NC [NC, NC]	73.944 [10.210, 535.55]	<.0001	
MOW	70	56 (80.0)	0.41 [0.30, 0.53]	67	3 (4.5)	NC [NC, NC]	23.311 [7.234, 75.123]	<.0001	
Age Category									
< 65	29	20 (69.0)	0.79 [0.30, 8.41]	28	0 (0.0)	NC [NC, NC]	NC [NC, NC]	<.0001	0.9790
>= 65	138	123 (89.1)	0.46 [0.36, 0.56]	131	4 (3.1)	NC [NC, NC]	38.369 [14.086, 104.51]	<.0001	
Sex									
Male	135	114 (84.4)	0.49 [0.33, 0.69]	120	4 (3.3)	NC [NC, NC]	29.510 [10.812, 80.544]	<.0001	0.9825
Female	32	29 (90.6)	0.46 [0.33, 0.53]	39	0 (0.0)	NC [NC, NC]	NC [NC, NC]	<.0001	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.61.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Alopecia (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	58 (34.7%)	0 (0.0%)	
Number of patients censored	109 (65.3%)	159 (100.0%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			NC [NC, NC]
Log-rank test			
Two-sided unstratified log-rank p-value			<.0001

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.61.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Alopecia (PT)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	46 (33.3)	NC [NC, NC]	129	0 (0.0)	NC [NC, NC]	NC [NC, NC]	<.0001	0.9999
Eligible but Declined	29	12 (41.4)	NC [1.18, NC]	30	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0183	
Tumor Stage									
T2N0	31	16 (51.6)	6.87 [1.18, NC]	27	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0092	1.0000
T3/T4aN0	129	40 (31.0)	NC [NC, NC]	125	0 (0.0)	NC [NC, NC]	NC [NC, NC]	<.0001	
T1-4aN1	7	2 (28.6)	NC [0.66, NC]	7	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.1413	
Geographical Regions									
US	21	11 (52.4)	2.07 [0.79, NC]	23	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0006	1.0000
EU	76	29 (38.2)	NC [5.82, NC]	69	0 (0.0)	NC [NC, NC]	NC [NC, NC]	<.0001	
MOW	70	18 (25.7)	NC [NC, NC]	67	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0030	
Age Category									
< 65	29	10 (34.5)	NC [5.82, NC]	28	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0226	1.0000
>= 65	138	48 (34.8)	NC [NC, NC]	131	0 (0.0)	NC [NC, NC]	NC [NC, NC]	<.0001	
Sex									
Male	135	38 (28.1)	NC [NC, NC]	120	0 (0.0)	NC [NC, NC]	NC [NC, NC]	<.0001	0.9995
Female	32	20 (62.5)	1.31 [0.79, 6.87]	39	0 (0.0)	NC [NC, NC]	NC [NC, NC]	<.0001	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.62.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Dry Skin (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	25 (15.0%)	1 (0.6%)	
Number of patients censored	142 (85.0%)	158 (99.4%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			6.659 [0.819, 54.126]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0403

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.62.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Dry Skin (PT)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	21 (15.2)	NC [NC, NC]	129	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0103	0.9895
Eligible but Declined	29	4 (13.8)	NC [NC, NC]	30	1 (3.3)	NC [NC, NC]	0.000 [0.000, NC]	0.3255	
Tumor Stage									
T2N0	31	5 (16.1)	NC [NC, NC]	27	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.1833	1.0000
T3/T4aN0	129	19 (14.7)	NC [NC, NC]	125	1 (0.8)	NC [NC, NC]	4.816 [0.563, 41.216]	0.1124	
T1-4aN1	7	1 (14.3)	NC [1.31, NC]	7	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	
Geographical Regions									
US	21	4 (19.0)	NC [NC, NC]	23	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.3061	0.9999
EU	76	11 (14.5)	NC [NC, NC]	69	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0542	
MOW	70	10 (14.3)	NC [NC, NC]	67	1 (1.5)	NC [NC, NC]	1.894 [0.172, 20.892]	0.5956	
Age Category									
< 65	29	3 (10.3)	NC [NC, NC]	28	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	0.9900
>= 65	138	22 (15.9)	NC [NC, NC]	131	1 (0.8)	NC [NC, NC]	6.638 [0.817, 53.954]	0.0407	
Sex									
Male	135	22 (16.3)	NC [NC, NC]	120	1 (0.8)	NC [NC, NC]	5.339 [0.643, 44.333]	0.0820	0.9922
Female	32	3 (9.4)	NC [9.43, NC]	39	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.2758	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.63.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Pruritus (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	79 (47.3%)	0 (0.0%)	
Number of patients censored	88 (52.7%)	159 (100.0%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	8.02 [4.73, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			NC [NC, NC]
Log-rank test			
Two-sided unstratified log-rank p-value			<.0001

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.63.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Pruritus (PT)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	64 (46.4)	9.17 [5.09, NC]	129	0 (0.0)	NC [NC, NC]	NC [NC, NC]	<.0001	1.0000
Eligible but Declined	29	15 (51.7)	6.18 [0.36, NC]	30	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0010	
Tumor Stage									
T2N0	31	15 (48.4)	5.62 [3.02, NC]	27	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0050	1.0000
T3/T4aN0	129	59 (45.7)	9.63 [4.57, NC]	125	0 (0.0)	NC [NC, NC]	NC [NC, NC]	<.0001	
T1-4aN1	7	5 (71.4)	5.55 [0.10, NC]	7	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.1413	
Geographical Regions									
US	21	13 (61.9)	5.55 [0.36, NC]	23	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0011	1.0000
EU	76	35 (46.1)	8.02 [4.63, NC]	69	0 (0.0)	NC [NC, NC]	NC [NC, NC]	<.0001	
MOW	70	31 (44.3)	NC [4.04, NC]	67	0 (0.0)	NC [NC, NC]	NC [NC, NC]	<.0001	
Age Category									
< 65	29	11 (37.9)	NC [1.41, NC]	28	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0030	0.9998
>= 65	138	68 (49.3)	5.62 [4.57, 10.02]	131	0 (0.0)	NC [NC, NC]	NC [NC, NC]	<.0001	
Sex									
Male	135	65 (48.1)	6.18 [4.63, NC]	120	0 (0.0)	NC [NC, NC]	NC [NC, NC]	<.0001	1.0000
Female	32	14 (43.8)	9.63 [0.49, NC]	39	0 (0.0)	NC [NC, NC]	NC [NC, NC]	<.0001	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.64.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Rash (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	42 (25.1%)	1 (0.6%)	
Number of patients censored	125 (74.9%)	158 (99.4%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			34.786 [4.758, 254.33]
Log-rank test			
Two-sided unstratified log-rank p-value			<.0001

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.64.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Rash (PT)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	34 (24.6)	NC [NC, NC]	129	0 (0.0)	NC [NC, NC]	NC [NC, NC]	<.0001	0.9880
Eligible but Declined	29	8 (27.6)	NC [9.63, NC]	30	1 (3.3)	NC [NC, NC]	5.679 [0.663, 48.636]	0.0736	
Tumor Stage									
T2N0	31	9 (29.0)	NC [5.95, NC]	27	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0049	0.9999
T3/T4aN0	129	30 (23.3)	NC [NC, NC]	125	1 (0.8)	NC [NC, NC]	23.210 [3.128, 172.21]	<.0001	
T1-4aN1	7	3 (42.9)	NC [0.13, NC]	7	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0597	
Geographical Regions									
US	21	2 (9.5)	NC [NC, NC]	23	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.1384	0.9998
EU	76	19 (25.0)	NC [NC, NC]	69	1 (1.4)	NC [NC, NC]	14.032 [1.845, 106.71]	0.0008	
MOW	70	21 (30.0)	NC [NC, NC]	67	0 (0.0)	NC [NC, NC]	NC [NC, NC]	<.0001	
Age Category									
< 65	29	6 (20.7)	NC [NC, NC]	28	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0832	0.9885
>= 65	138	36 (26.1)	NC [NC, NC]	131	1 (0.8)	NC [NC, NC]	31.871 [4.346, 233.72]	<.0001	
Sex									
Male	135	34 (25.2)	NC [NC, NC]	120	1 (0.8)	NC [NC, NC]	26.667 [3.623, 196.27]	<.0001	0.9907
Female	32	8 (25.0)	NC [9.63, NC]	39	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0050	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.65.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Rash Maculo-Papular (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	27 (16.2%)	0 (0.0%)	
Number of patients censored	140 (83.8%)	159 (100.0%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			NC [NC, NC]
Log-rank test			
Two-sided unstratified log-rank p-value			<.0001

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.65.1.2: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Rash Maculo-Papular (PT)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	18 (13.0)	NC [NC, NC]	129	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0004	0.9997
Eligible but Declined	29	9 (31.0)	NC [5.59, NC]	30	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0091	
Tumor Stage									
T2N0	31	5 (16.1)	NC [NC, NC]	27	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0556	1.0000
T3/T4aN0	129	20 (15.5)	NC [NC, NC]	125	0 (0.0)	NC [NC, NC]	NC [NC, NC]	<.0001	
T1-4aN1	7	2 (28.6)	NC [1.08, NC]	7	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	
Geographical Regions									
US	21	15 (71.4)	1.08 [0.43, 6.70]	23	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0002	1.0000
EU	76	6 (7.9)	NC [NC, NC]	69	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0308	
MOW	70	6 (8.6)	NC [NC, NC]	67	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0483	
Age Category									
< 65	29	4 (13.8)	NC [NC, NC]	28	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0832	0.9999
>= 65	138	23 (16.7)	NC [NC, NC]	131	0 (0.0)	NC [NC, NC]	NC [NC, NC]	<.0001	
Sex									
Male	135	20 (14.8)	NC [NC, NC]	120	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0009	0.9999
Female	32	7 (21.9)	NC [NC, NC]	39	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0024	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.66.1.1: Time to Event Analysis of Treatment Emergent Adverse Events in Combined Treatment Phases - Vascular Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	27 (16.2%)	12 (7.5%)	
Number of patients censored	140 (83.8%)	147 (92.5%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	1.38 [1.38, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.707 [0.299, 1.672]
Log-rank test			
Two-sided unstratified log-rank p-value			0.4293

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.67.1.1: Time to Event Analysis of Severe Treatment Emergent Adverse Events in Combined Treatment Phases - Blood and Lymphatic System Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	27 (16.2%)	10 (6.3%)	
Number of patients censored	140 (83.8%)	149 (93.7%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			1.110 [0.479, 2.568]
Log-rank test			
Two-sided unstratified log-rank p-value			0.8059

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.68.1.1: Time to Event Analysis of Severe Treatment Emergent Adverse Events in Combined Treatment Phases - Anaemia (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	15 (9.0%)	10 (6.3%)	
Number of patients censored	152 (91.0%)	149 (93.7%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.275 [0.076, 0.999]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0357

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.68.1.2: Time to Event Analysis of Severe Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Anaemia (PT)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	15 (10.9)	NC [NC, NC]	129	9 (7.0)	NC [NC, NC]	0.298 [0.081, 1.101]	0.0539	0.9888
Eligible but Declined	29	0 (0.0)	NC [NC, NC]	30	1 (3.3)	NC [NC, NC]	NC [NC, NC]	0.3255	
Tumor Stage									
T2N0	31	4 (12.9)	NC [NC, NC]	27	1 (3.7)	NC [NC, NC]	0.000 [0.000, NC]	0.2839	0.6301
T3/T4aN0	129	11 (8.5)	NC [NC, NC]	125	9 (7.2)	NC [NC, NC]	0.309 [0.084, 1.141]	0.0621	
T1-4aN1	7	0 (0.0)	NC [NC, NC]	7	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	
Geographical Regions									
US	21	2 (9.5)	NC [NC, NC]	23	1 (4.3)	NC [NC, NC]	1.047 [0.065, 16.744]	0.9743	0.7583
EU	76	7 (9.2)	NC [NC, NC]	69	6 (8.7)	NC [NC, NC]	0.145 [0.017, 1.204]	0.0377	
MOW	70	6 (8.6)	NC [NC, NC]	67	3 (4.5)	NC [NC, NC]	0.315 [0.033, 3.031]	0.2910	
Age Category									
< 65	29	1 (3.4)	NC [NC, NC]	28	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	0.9909
>= 65	138	14 (10.1)	NC [NC, NC]	131	10 (7.6)	NC [NC, NC]	0.272 [0.075, 0.987]	0.0339	
Sex									
Male	135	11 (8.1)	NC [NC, NC]	120	6 (5.0)	NC [NC, NC]	0.289 [0.058, 1.430]	0.1054	0.7539
Female	32	4 (12.5)	NC [NC, NC]	39	4 (10.3)	NC [NC, NC]	0.284 [0.032, 2.540]	0.2277	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.69.1.1: Time to Event Analysis of Severe Treatment Emergent Adverse Events in Combined Treatment Phases - Neutropenia (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	10 (6.0%)	0 (0.0%)	
Number of patients censored	157 (94.0%)	159 (100.0%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			NC [NC, NC]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0170

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.69.1.2: Time to Event Analysis of Severe Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Neutropenia (PT)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	9 (6.5)		129	0 (0.0)				
Eligible but Declined	29	1 (3.4)		30	0 (0.0)				
Tumor Stage									
T2N0	31	1 (3.2)		27	0 (0.0)				
T3/T4aN0	129	8 (6.2)		125	0 (0.0)				
T1-4aN1	7	1 (14.3)		7	0 (0.0)				
Geographical Regions									
US	21	0 (0.0)		23	0 (0.0)				
EU	76	6 (7.9)		69	0 (0.0)				
MOW	70	4 (5.7)		67	0 (0.0)				
Age Category									
< 65	29	1 (3.4)		28	0 (0.0)				
>= 65	138	9 (6.5)		131	0 (0.0)				
Sex									
Male	135	8 (5.9)		120	0 (0.0)				
Female	32	2 (6.3)		39	0 (0.0)				

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.70.1.1: Time to Event Analysis of Severe Treatment Emergent Adverse Events in Combined Treatment Phases - Gastrointestinal Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	31 (18.6%)	16 (10.1%)	
Number of patients censored	136 (81.4%)	143 (89.9%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [15.54, NC]	1.12 [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.229 [0.077, 0.680]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0038

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.70.1.2: Time to Event Analysis of Severe Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Gastrointestinal Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	27 (19.6)	NC [15.54, NC]	129	15 (11.6)	1.12 [NC, NC]	0.180 [0.053, 0.611]	0.0020	0.5206
Eligible but Declined	29	4 (13.8)	NC [NC, NC]	30	1 (3.3)	NC [NC, NC]	1.017 [0.064, 16.262]	0.9904	
Tumor Stage									
T2N0	31	8 (25.8)	NC [12.32, NC]	27	1 (3.7)	NC [NC, NC]	0.885 [0.055, 14.152]	0.9314	0.3074
T3/T4aN0	129	21 (16.3)	NC [15.54, NC]	125	15 (12.0)	1.12 [NC, NC]	0.186 [0.055, 0.633]	0.0026	
T1-4aN1	7	2 (28.6)	NC [3.09, NC]	7	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	
Geographical Regions									
US	21	9 (42.9)	8.05 [2.89, NC]	23	5 (21.7)	1.12 [NC, NC]	0.084 [0.006, 1.108]	0.0353	0.6663
EU	76	15 (19.7)	NC [NC, NC]	69	9 (13.0)	NC [NC, NC]	0.288 [0.078, 1.063]	0.0469	
MOW	70	7 (10.0)	NC [15.54, NC]	67	2 (3.0)	NC [NC, NC]	0.464 [0.042, 5.118]	0.5224	
Age Category									
< 65	29	4 (13.8)	NC [NC, NC]	28	2 (7.1)	NC [NC, NC]	0.000 [0.000, NC]	0.1464	0.7772
>= 65	138	27 (19.6)	NC [15.54, NC]	131	14 (10.7)	1.12 [NC, NC]	0.260 [0.086, 0.784]	0.0102	
Sex									
Male	135	26 (19.3)	NC [15.54, NC]	120	12 (10.0)	NC [NC, NC]	0.212 [0.060, 0.753]	0.0082	0.7912
Female	32	5 (15.6)	NC [NC, NC]	39	4 (10.3)	1.12 [NC, NC]	0.324 [0.043, 2.443]	0.2559	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.71.1.1: Time to Event Analysis of Severe Treatment Emergent Adverse Events in Combined Treatment Phases - General Disorders and Administration Site Conditions (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	13 (7.8%)	10 (6.3%)	
Number of patients censored	154 (92.2%)	149 (93.7%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	2.40 [1.54, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.214 [0.055, 0.839]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0170

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.71.1.2: Time to Event Analysis of Severe Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - General Disorders and Administration Site Conditions (SOC)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	13 (9.4)	NC [NC, NC]	129	8 (6.2)	1.54 [1.54, NC]	0.358 [0.099, 1.294]	0.1028	0.9884
Eligible but Declined	29	0 (0.0)	NC [NC, NC]	30	2 (6.7)	2.50 [NC, NC]	NC [NC, NC]	0.0062	
Tumor Stage									
T2N0	31	5 (16.1)	NC [13.57, NC]	27	2 (7.4)	2.40 [NC, NC]	0.178 [0.013, 2.457]	0.1869	0.6271
T3/T4aN0	129	8 (6.2)	NC [NC, NC]	125	8 (6.4)	1.54 [1.54, NC]	0.248 [0.056, 1.093]	0.0477	
T1-4aN1	7	0 (0.0)	NC [NC, NC]	7	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	
Geographical Regions									
US	21	1 (4.8)	NC [NC, NC]	23	1 (4.3)	NC [NC, NC]	1.071 [0.067, 17.129]	0.9612	0.8648
EU	76	9 (11.8)	NC [NC, NC]	69	6 (8.7)	1.54 [1.54, NC]	0.336 [0.077, 1.461]	0.1305	
MOW	70	3 (4.3)	NC [NC, NC]	67	3 (4.5)	2.50 [NC, NC]	0.000 [0.000, NC]	0.0049	
Age Category									
< 65	29	2 (6.9)	NC [NC, NC]	28	1 (3.6)	NC [NC, NC]	0.000 [0.000, NC]	0.3088	0.8934
>= 65	138	11 (8.0)	NC [NC, NC]	131	9 (6.9)	2.40 [1.54, NC]	0.241 [0.061, 0.945]	0.0296	
Sex									
Male	135	8 (5.9)	NC [NC, NC]	120	9 (7.5)	2.40 [1.54, NC]	0.034 [0.006, 0.216]	0.0003	0.0599
Female	32	5 (15.6)	NC [13.57, NC]	39	1 (2.6)	NC [NC, NC]	3.630 [0.378, 34.898]	0.2319	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.72.1.1: Time to Event Analysis of Severe Treatment Emergent Adverse Events in Combined Treatment Phases - Infections and Infestations (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	55 (32.9%)	43 (27.0%)	
Number of patients censored	112 (67.1%)	116 (73.0%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [11.20, NC]	1.61 [1.15, 1.91]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.037 [0.017, 0.081]
Log-rank test			
Two-sided unstratified log-rank p-value			<.0001

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.72.1.2: Time to Event Analysis of Severe Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Infections and Infestations (SOC)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	47 (34.1)	NC [9.76, NC]	129	37 (28.7)	1.41 [1.15, 1.87]	0.036 [0.016, 0.084]	<.0001	0.9040
Eligible but Declined	29	8 (27.6)	NC [9.79, NC]	30	6 (20.0)	2.00 [2.00, NC]	0.051 [0.008, 0.315]	0.0006	
Tumor Stage									
T2N0	31	11 (35.5)	NC [4.24, NC]	27	6 (22.2)	1.15 [1.15, NC]	0.032 [0.005, 0.194]	<.0001	0.7309
T3/T4aN0	129	41 (31.8)	NC [13.37, NC]	125	34 (27.2)	1.84 [1.08, 2.69]	0.042 [0.017, 0.103]	<.0001	
T1-4aN1	7	3 (42.9)	6.77 [3.68, NC]	7	3 (42.9)	1.91 [0.39, NC]	0.000 [0.000, NC]	0.0032	
Geographical Regions									
US	21	6 (28.6)	NC [4.67, NC]	23	7 (30.4)	1.38 [1.38, NC]	0.000 [0.000, NC]	0.0002	0.7520
EU	76	24 (31.6)	NC [9.79, NC]	69	20 (29.0)	1.61 [1.15, 2.69]	0.046 [0.016, 0.130]	<.0001	
MOW	70	25 (35.7)	NC [7.79, NC]	67	16 (23.9)	1.84 [1.08, NC]	0.044 [0.012, 0.163]	<.0001	
Age Category									
< 65	29	12 (41.4)	NC [4.47, NC]	28	6 (21.4)	1.87 [1.87, NC]	0.060 [0.008, 0.424]	0.0033	0.5402
>= 65	138	43 (31.2)	NC [10.28, NC]	131	37 (28.2)	1.41 [1.15, 1.91]	0.037 [0.016, 0.084]	<.0001	
Sex									
Male	135	46 (34.1)	NC [11.20, NC]	120	32 (26.7)	1.41 [1.15, 2.00]	0.043 [0.019, 0.098]	<.0001	0.7941
Female	32	9 (28.1)	NC [5.26, NC]	39	11 (28.2)	1.84 [1.08, NC]	0.019 [0.002, 0.179]	<.0001	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.73.1.1: Time to Event Analysis of Severe Treatment Emergent Adverse Events in Combined Treatment Phases - Urinary Tract Infection (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	20 (12.0%)	17 (10.7%)	
Number of patients censored	147 (88.0%)	142 (89.3%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	1.84 [1.08, 2.76]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.025 [0.008, 0.077]
Log-rank test			
Two-sided unstratified log-rank p-value			<.0001

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.73.1.2: Time to Event Analysis of Severe Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Urinary Tract Infection (PT)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	19 (13.8)	NC [NC, NC]	129	14 (10.9)	1.84 [1.08, 2.76]	0.026 [0.008, 0.089]	<.0001	0.1993
Eligible but Declined	29	1 (3.4)	NC [NC, NC]	30	3 (10.0)	2.00 [NC, NC]	0.032 [0.002, 0.438]	0.0106	
Tumor Stage									
T2N0	31	5 (16.1)	NC [NC, NC]	27	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	0.8891
T3/T4aN0	129	14 (10.9)	NC [NC, NC]	125	16 (12.8)	1.84 [1.08, 2.76]	0.027 [0.008, 0.090]	<.0001	
T1-4aN1	7	1 (14.3)	NC [7.92, NC]	7	1 (14.3)	2.00 [NC, NC]	0.000 [0.000, NC]	0.0082	
Geographical Regions									
US	21	3 (14.3)	NC [7.92, NC]	23	1 (4.3)	NC [NC, NC]	0.000 [0.000, NC]	0.3393	0.5153
EU	76	10 (13.2)	NC [NC, NC]	69	8 (11.6)	2.69 [1.08, NC]	0.036 [0.008, 0.172]	<.0001	
MOW	70	7 (10.0)	NC [NC, NC]	67	8 (11.9)	1.84 [1.08, NC]	0.026 [0.006, 0.123]	<.0001	
Age Category									
< 65	29	5 (17.2)	NC [NC, NC]	28	3 (10.7)	2.00 [NC, NC]	0.031 [0.002, 0.425]	0.0092	0.9068
>= 65	138	15 (10.9)	NC [NC, NC]	131	14 (10.7)	1.84 [1.08, 2.76]	0.027 [0.008, 0.091]	<.0001	
Sex									
Male	135	18 (13.3)	NC [NC, NC]	120	12 (10.0)	2.69 [1.08, NC]	0.029 [0.008, 0.102]	<.0001	0.2980
Female	32	2 (6.3)	NC [NC, NC]	39	5 (12.8)	1.61 [1.08, NC]	0.027 [0.003, 0.290]	0.0009	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.74.1.1: Time to Event Analysis of Severe Treatment Emergent Adverse Events in Combined Treatment Phases - Injury, Poisoning and Procedural Complications (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	10 (6.0%)	12 (7.5%)	
Number of patients censored	157 (94.0%)	147 (92.5%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	1.87 [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.000 [0.000, NC]
Log-rank test			
Two-sided unstratified log-rank p-value			<.0001

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.74.1.2: Time to Event Analysis of Severe Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Injury, Poisoning and Procedural Complications (SOC)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	7 (5.1)	NC [NC, NC]	129	10 (7.8)	1.87 [NC, NC]	0.000 [0.000, NC]	0.0001	0.4878
Eligible but Declined	29	3 (10.3)	NC [NC, NC]	30	2 (6.7)	NC [NC, NC]	0.000 [0.000, NC]	0.1608	
Tumor Stage									
T2N0	31	1 (3.2)	NC [NC, NC]	27	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	1.0000
T3/T4aN0	129	9 (7.0)	NC [NC, NC]	125	11 (8.8)	1.87 [NC, NC]	0.000 [0.000, NC]	<.0001	
T1-4aN1	7	0 (0.0)	NC [NC, NC]	7	1 (14.3)	NC [0.23, NC]	NC [NC, NC]	0.3173	
Geographical Regions									
US	21	1 (4.8)	NC [NC, NC]	23	2 (8.7)	NC [NC, NC]	0.000 [0.000, NC]	0.1715	0.7993
EU	76	7 (9.2)	NC [NC, NC]	69	6 (8.7)	NC [NC, NC]	0.000 [0.000, NC]	0.0088	
MOW	70	2 (2.9)	NC [NC, NC]	67	4 (6.0)	1.87 [NC, NC]	0.000 [0.000, NC]	0.0037	
Age Category									
< 65	29	4 (13.8)	NC [NC, NC]	28	1 (3.6)	NC [NC, NC]	0.000 [0.000, NC]	0.3088	0.1525
>= 65	138	6 (4.3)	NC [NC, NC]	131	11 (8.4)	1.87 [NC, NC]	0.000 [0.000, NC]	<.0001	
Sex									
Male	135	9 (6.7)	NC [NC, NC]	120	7 (5.8)	NC [NC, NC]	0.000 [0.000, NC]	0.0045	0.2777
Female	32	1 (3.1)	NC [NC, NC]	39	5 (12.8)	1.87 [NC, NC]	0.000 [0.000, NC]	0.0053	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.75.1.1: Time to Event Analysis of Severe Treatment Emergent Adverse Events in Combined Treatment Phases - Investigations (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	16 (9.6%)	1 (0.6%)	
Number of patients censored	151 (90.4%)	158 (99.4%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			1.872 [0.170, 20.641]
Log-rank test			
Two-sided unstratified log-rank p-value			0.6028

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.76.1.1: Time to Event Analysis of Severe Treatment Emergent Adverse Events in Combined Treatment Phases - Metabolism and Nutrition Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	26 (15.6%)	4 (2.5%)	
Number of patients censored	141 (84.4%)	155 (97.5%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	2.56 [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			2.403 [0.755, 7.651]
Log-rank test			
Two-sided unstratified log-rank p-value			0.1261

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.77.1.1: Time to Event Analysis of Severe Treatment Emergent Adverse Events in Combined Treatment Phases - Renal and Urinary Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	19 (11.4%)	8 (5.0%)	
Number of patients censored	148 (88.6%)	151 (95.0%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	1.41 [1.41, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.032 [0.007, 0.146]
Log-rank test			
Two-sided unstratified log-rank p-value			<.0001

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.77.1.2: Time to Event Analysis of Severe Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Renal and Urinary Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	18 (13.0)	NC [NC, NC]	129	8 (6.2)	1.41 [1.41, NC]	0.034 [0.007, 0.160]	<.0001	0.9902
Eligible but Declined	29	1 (3.4)	NC [NC, NC]	30	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	
Tumor Stage									
T2N0	31	1 (3.2)	NC [NC, NC]	27	1 (3.7)	1.41 [NC, NC]	0.000 [0.000, NC]	<.0001	0.8107
T3/T4aN0	129	16 (12.4)	NC [NC, NC]	125	7 (5.6)	1.54 [1.41, NC]	0.057 [0.011, 0.306]	0.0017	
T1-4aN1	7	2 (28.6)	NC [6.77, NC]	7	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	
Geographical Regions									
US	21	2 (9.5)	NC [8.05, NC]	23	2 (8.7)	2.43 [NC, NC]	0.159 [0.007, 3.472]	0.2271	0.4884
EU	76	7 (9.2)	NC [NC, NC]	69	4 (5.8)	1.41 [NC, NC]	0.012 [0.001, 0.178]	0.0037	
MOW	70	10 (14.3)	NC [NC, NC]	67	2 (3.0)	1.48 [1.41, NC]	0.021 [0.001, 0.323]	0.0068	
Age Category									
< 65	29	1 (3.4)	NC [NC, NC]	28	1 (3.6)	NC [NC, NC]	0.000 [0.000, NC]	0.3088	0.2695
>= 65	138	18 (13.0)	NC [NC, NC]	131	7 (5.3)	1.41 [1.41, NC]	0.039 [0.009, 0.178]	0.0002	
Sex									
Male	135	13 (9.6)	NC [NC, NC]	120	3 (2.5)	1.54 [1.54, NC]	0.110 [0.009, 1.408]	0.0817	0.3495
Female	32	6 (18.8)	NC [7.56, NC]	39	5 (12.8)	1.41 [NC, NC]	0.024 [0.002, 0.253]	0.0008	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.78.1.1: Time to Event Analysis of Severe Treatment Emergent Adverse Events in Combined Treatment Phases - Skin and Subcutaneous Tissue Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	27 (16.2%)	0 (0.0%)	
Number of patients censored	140 (83.8%)	159 (100.0%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			NC [NC, NC]
Log-rank test			
Two-sided unstratified log-rank p-value			<.0001

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.78.1.2: Time to Event Analysis of Severe Treatment Emergent Adverse Events in Combined Treatment Phases by Subgroups - Skin and Subcutaneous Tissue Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	22 (15.9)	NC [NC, NC]	129	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0004	1.0000
Eligible but Declined	29	5 (17.2)	NC [NC, NC]	30	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0729	
Tumor Stage									
T2N0	31	5 (16.1)	NC [NC, NC]	27	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.1830	1.0000
T3/T4aN0	129	21 (16.3)	NC [NC, NC]	125	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0002	
T1-4aN1	7	1 (14.3)	NC [8.77, NC]	7	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	
Geographical Regions									
US	21	4 (19.0)	NC [7.16, NC]	23	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.2953	1.0000
EU	76	11 (14.5)	NC [NC, NC]	69	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0176	
MOW	70	12 (17.1)	NC [NC, NC]	67	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0026	
Age Category									
< 65	29	2 (6.9)	NC [NC, NC]	28	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.3258	0.9998
>= 65	138	25 (18.1)	NC [NC, NC]	131	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0001	
Sex									
Male	135	23 (17.0)	NC [NC, NC]	120	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0005	0.9999
Female	32	4 (12.5)	NC [NC, NC]	39	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0530	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 30 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.79.1.1: Time to Event Analysis of Treatment Emergent Serious Adverse Events in Combined Treatment Phases - Gastrointestinal Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	21 (12.6%)	12 (7.5%)	
Number of patients censored	146 (87.4%)	147 (92.5%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.978 [0.446, 2.144]
Log-rank test			
Two-sided unstratified log-rank p-value			0.9560

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 90 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.80.1.1: Time to Event Analysis of Treatment Emergent Serious Adverse Events in Combined Treatment Phases - General Disorders and Administration Site Conditions (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	9 (5.4%)	8 (5.0%)	
Number of patients censored	158 (94.6%)	151 (95.0%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.463 [0.140, 1.539]
Log-rank test			
Two-sided unstratified log-rank p-value			0.1979

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 90 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.81.1.1: Time to Event Analysis of Treatment Emergent Serious Adverse Events in Combined Treatment Phases - Infections and Infestations (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	49 (29.3%)	37 (23.3%)	
Number of patients censored	118 (70.7%)	122 (76.7%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.317 [0.172, 0.587]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0001

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 90 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.81.1.2: Time to Event Analysis of Treatment Emergent Serious Adverse Events in Combined Treatment Phases by Subgroups - Infections and Infestations (SOC)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	42 (30.4)	NC [13.83, NC]	129	33 (25.6)	NC [NC, NC]	0.270 [0.136, 0.534]	<.0001	0.5715
Eligible but Declined	29	7 (24.1)	NC [NC, NC]	30	4 (13.3)	NC [NC, NC]	0.741 [0.166, 3.314]	0.6943	
Tumor Stage									
T2N0	31	10 (32.3)	NC [7.59, NC]	27	6 (22.2)	NC [NC, NC]	0.518 [0.146, 1.838]	0.3023	0.8776
T3/T4aN0	129	36 (27.9)	NC [NC, NC]	125	28 (22.4)	NC [NC, NC]	0.306 [0.149, 0.631]	0.0007	
T1-4aN1	7	3 (42.9)	7.92 [3.68, NC]	7	3 (42.9)	NC [0.39, NC]	0.000 [0.000, NC]	0.0597	
Geographical Regions									
US	21	4 (19.0)	NC [13.83, NC]	23	6 (26.1)	NC [1.91, NC]	0.152 [0.018, 1.267]	0.0447	0.3453
EU	76	23 (30.3)	NC [10.28, NC]	69	19 (27.5)	NC [NC, NC]	0.212 [0.079, 0.569]	0.0007	
MOW	70	22 (31.4)	NC [14.06, NC]	67	12 (17.9)	NC [NC, NC]	0.576 [0.235, 1.409]	0.2219	
Age Category									
< 65	29	11 (37.9)	NC [8.28, NC]	28	6 (21.4)	NC [NC, NC]	0.445 [0.111, 1.780]	0.2394	0.6150
>= 65	138	38 (27.5)	NC [NC, NC]	131	31 (23.7)	NC [NC, NC]	0.295 [0.148, 0.586]	0.0002	
Sex									
Male	135	42 (31.1)	NC [14.06, NC]	120	27 (22.5)	NC [NC, NC]	0.411 [0.216, 0.784]	0.0053	0.3587
Female	32	7 (21.9)	NC [9.79, NC]	39	10 (25.6)	NC [NC, NC]	0.000 [0.000, NC]	0.0020	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 90 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.82.1.1: Time to Event Analysis of Treatment Emergent Serious Adverse Events in Combined Treatment Phases - Urinary Tract Infection (PT)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	17 (10.2%)	15 (9.4%)	
Number of patients censored	150 (89.8%)	144 (90.6%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.357 [0.139, 0.921]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0261

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 90 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.82.1.2: Time to Event Analysis of Treatment Emergent Serious Adverse Events in Combined Treatment Phases by Subgroups - Urinary Tract Infection (PT)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	16 (11.6)	NC [NC, NC]	129	13 (10.1)	NC [NC, NC]	0.334 [0.119, 0.937]	0.0287	0.4816
Eligible but Declined	29	1 (3.4)	NC [NC, NC]	30	2 (6.7)	NC [NC, NC]	0.512 [0.046, 5.643]	0.5772	
Tumor Stage									
T2N0	31	4 (12.9)	NC [NC, NC]	27	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.3507	0.9921
T3/T4aN0	129	12 (9.3)	NC [NC, NC]	125	14 (11.2)	NC [NC, NC]	0.321 [0.115, 0.890]	0.0214	
T1-4aN1	7	1 (14.3)	NC [7.92, NC]	7	1 (14.3)	NC [2.00, NC]	0.000 [0.000, NC]	0.3173	
Geographical Regions									
US	21	2 (9.5)	NC [13.83, NC]	23	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	0.9126
EU	76	9 (11.8)	NC [NC, NC]	69	8 (11.6)	NC [NC, NC]	0.218 [0.046, 1.025]	0.0338	
MOW	70	6 (8.6)	NC [NC, NC]	67	7 (10.4)	NC [NC, NC]	0.499 [0.146, 1.704]	0.2574	
Age Category									
< 65	29	5 (17.2)	NC [NC, NC]	28	3 (10.7)	NC [NC, NC]	0.307 [0.032, 2.951]	0.2787	0.6981
>= 65	138	12 (8.7)	NC [NC, NC]	131	12 (9.2)	NC [NC, NC]	0.371 [0.131, 1.052]	0.0521	
Sex									
Male	135	17 (12.6)	NC [NC, NC]	120	10 (8.3)	NC [NC, NC]	0.510 [0.185, 1.402]	0.1835	0.9866
Female	32	0 (0.0)	NC [NC, NC]	39	5 (12.8)	NC [NC, NC]	NC [NC, NC]	0.0324	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 90 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.83.1.1: Time to Event Analysis of Treatment Emergent Serious Adverse Events in Combined Treatment Phases - Injury, Poisoning and Procedural Complications (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	11 (6.6%)	7 (4.4%)	
Number of patients censored	156 (93.4%)	152 (95.6%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.260 [0.054, 1.253]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0703

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 90 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.84.1.1: Time to Event Analysis of Treatment Emergent Serious Adverse Events in Combined Treatment Phases - Neoplasms Benign, Malignant and Unspecified (Incl Cysts and Polyps) (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	9 (5.4%)	4 (2.5%)	
Number of patients censored	158 (94.6%)	155 (97.5%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			1.387 [0.391, 4.914]
Log-rank test			
Two-sided unstratified log-rank p-value			0.6068

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 90 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.85.1.1: Time to Event Analysis of Treatment Emergent Serious Adverse Events in Combined Treatment Phases - Renal and Urinary Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	19 (11.4%)	8 (5.0%)	
Number of patients censored	148 (88.6%)	151 (95.0%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			0.694 [0.241, 1.999]
Log-rank test			
Two-sided unstratified log-rank p-value			0.4962

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 90 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2001.86.1.1: Time to Event Analysis of Treatment Emergent Serious Adverse Events in Combined Treatment Phases - Skin and Subcutaneous Tissue Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N= 167)	RC + PLND (N= 159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	10 (6.0%)	0 (0.0%)	
Number of patients censored	157 (94.0%)	159 (100.0%)	
Kaplan-Meier estimates of time to event (months)			
Quartiles, 95% CI (a)			
50%	NC [NC, NC]	NC [NC, NC]	
Difference in median			NC
Cox proportional hazards model			
Unstratified HR, 95% CI			NC [NC, NC]
Log-rank test			
Two-sided unstratified log-rank p-value			0.0018

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 90 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

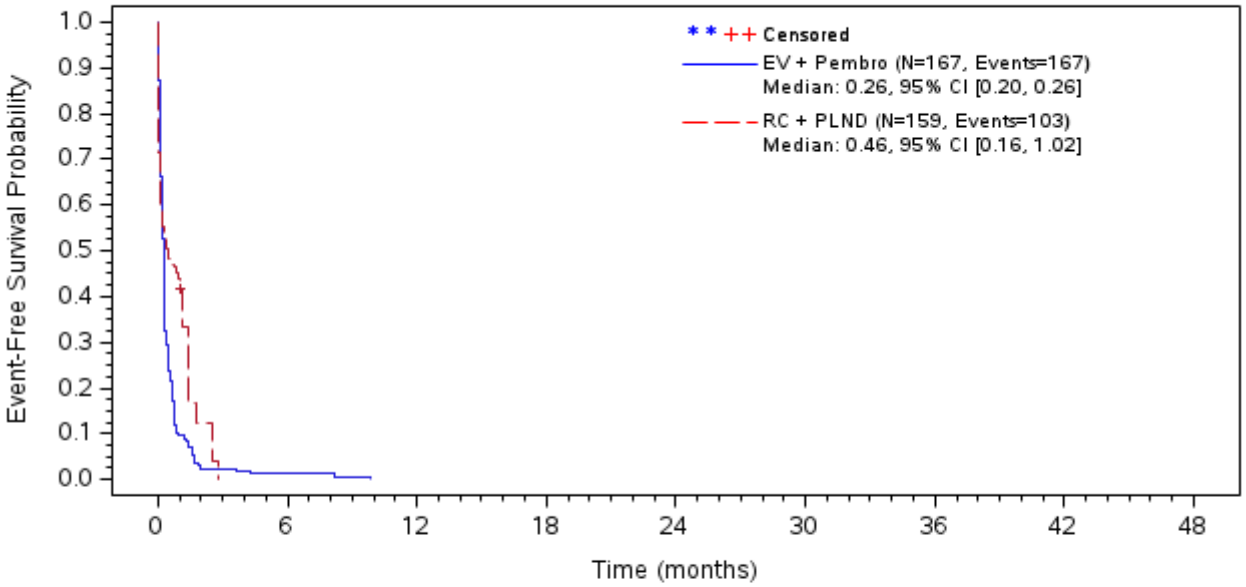
Table 303.1.2001.86.1.2: Time to Event Analysis of Treatment Emergent Serious Adverse Events in Combined Treatment Phases by Subgroups - Skin and Subcutaneous Tissue Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro			RC + PLND			EV + Pembro vs. RC + PLND		
Subgroup	N	n (%)	KME [95% CI](a)	N	n (%)	KME [95% CI](a)	HR [95% CI](b)	Log-rank p-value(c)	Test for Interaction p-value(d)
Cisplatin Eligibility									
Ineligible	138	10 (7.2)	NC [NC, NC]	129	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0019	0.9979
Eligible but Declined	29	0 (0.0)	NC [NC, NC]	30	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	
Tumor Stage									
T2N0	31	1 (3.2)		27	0 (0.0)				
T3/T4aN0	129	9 (7.0)		125	0 (0.0)				
T1-4aN1	7	0 (0.0)		7	0 (0.0)				
Geographical Regions									
US	21	0 (0.0)		23	0 (0.0)				
EU	76	4 (5.3)		69	0 (0.0)				
MOW	70	6 (8.6)		67	0 (0.0)				
Age Category									
< 65	29	0 (0.0)	NC [NC, NC]	28	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC	0.9979
>= 65	138	10 (7.2)	NC [NC, NC]	131	0 (0.0)	NC [NC, NC]	NC [NC, NC]	0.0018	
Sex									
Male	135	9 (6.7)		120	0 (0.0)				
Female	32	1 (3.1)		39	0 (0.0)				

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; HR=hazard ratio; KME=kaplan-meier estimate of time to event (months); N=number of patients; n=number of patients with events; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Based on the Brookmeyer-Crowley Method; (b) Calculated from Cox proportional hazards model; (c) Two-sided unstratified log-rank p-value; (d) Two-sided Type 3 Wald test p-value from Cox proportional hazards model including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
Time to event duration is defined as date of first exposure to treatment to start date of first AE + 1 day. Censoring date is defined as min(date of last dose of study treatment + 90 days, death date).
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
Subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 patients in each subgroup factor/level, and 2) at least 10 patients with events occurred in at least one of the subgroup factors/levels.
Only SOCs and PTs with significant treatment effect (p-value <0.05) in the overall SAF2 analysis set are presented.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Endpunkt: Unerwünschte Ereignisse; Ereigniszeitanalysen, Abbildungen

Figure 303.1.2001.1.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - SAF2 Analysis Set



at Risk (% Censored)

1	167 (0.0)	2 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
3	159 (0.0)	0 (35.2)	0 (35.2)	0 (35.2)	0 (35.2)	0 (35.2)	0 (35.2)	0 (35.2)	0 (35.2)

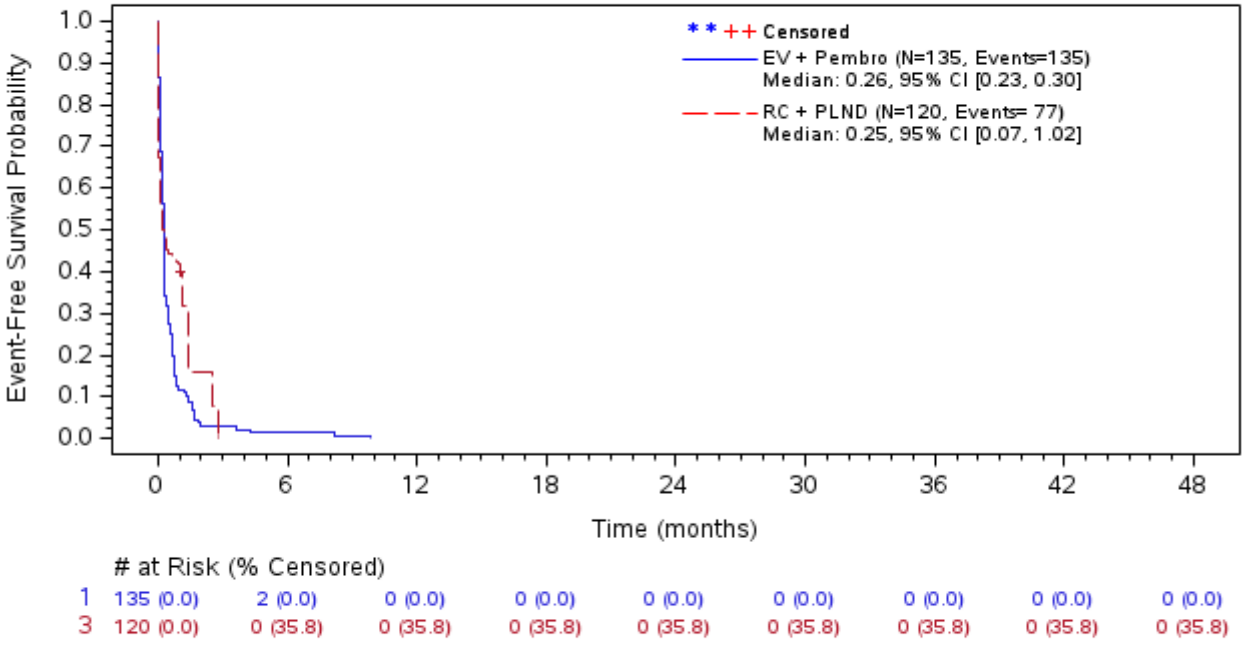
Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

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Figure 303.1.2001.1.1.5: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases by Sex - SAF2 Analysis Set

Sex: Male



at Risk (% Censored)

1	135 (0.0)	2 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
3	120 (0.0)	0 (35.8)	0 (35.8)	0 (35.8)	0 (35.8)	0 (35.8)	0 (35.8)	0 (35.8)	0 (35.8)

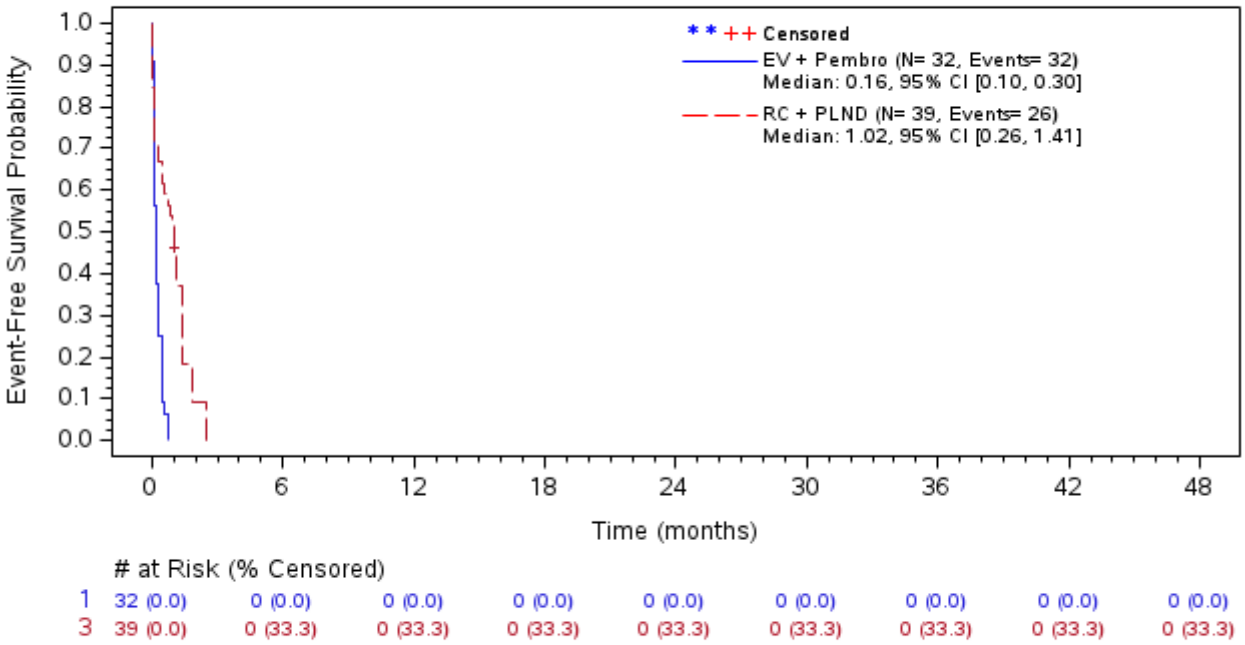
Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.1.1.5: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases by Sex - SAF2 Analysis Set

Sex: Female



at Risk (% Censored)

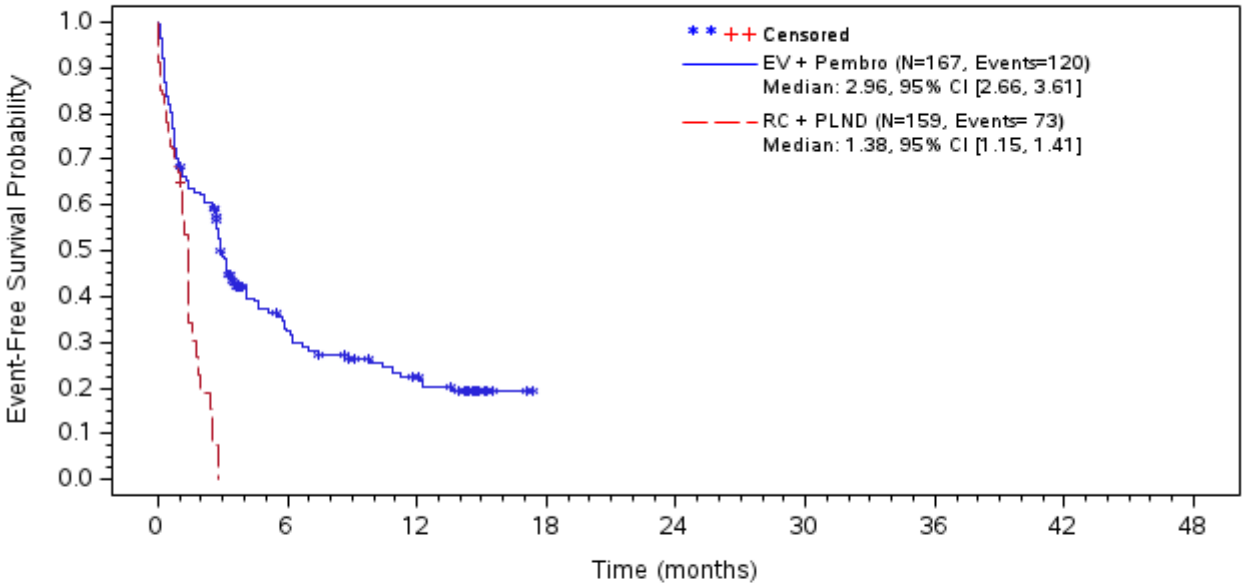
1	32 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
3	39 (0.0)	0 (33.3)	0 (33.3)	0 (33.3)	0 (33.3)	0 (33.3)	0 (33.3)	0 (33.3)	0 (33.3)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.2.1: Kaplan-Meier Plot of Time to Severe Treatment Emergent Adverse Events in Combined Treatment Phases - SAF2 Analysis Set



at Risk (% Censored)

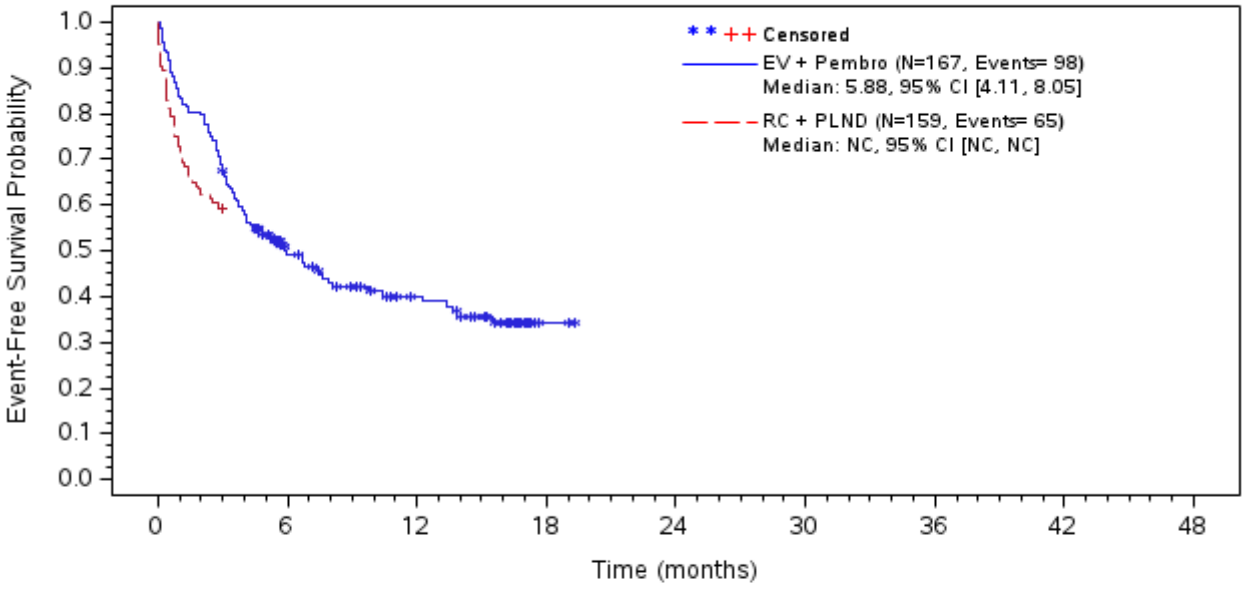
1	167 (0.0)	39 (13.2)	22 (16.8)	0 (28.1)	0 (28.1)	0 (28.1)	0 (28.1)	0 (28.1)	0 (28.1)
3	159 (0.0)	0 (54.1)	0 (54.1)	0 (54.1)	0 (54.1)	0 (54.1)	0 (54.1)	0 (54.1)	0 (54.1)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.3.1: Kaplan-Meier Plot of Time to Treatment Emergent Serious Adverse Events in Combined Treatment Phases - SAF2 Analysis Set



at Risk (% Censored)

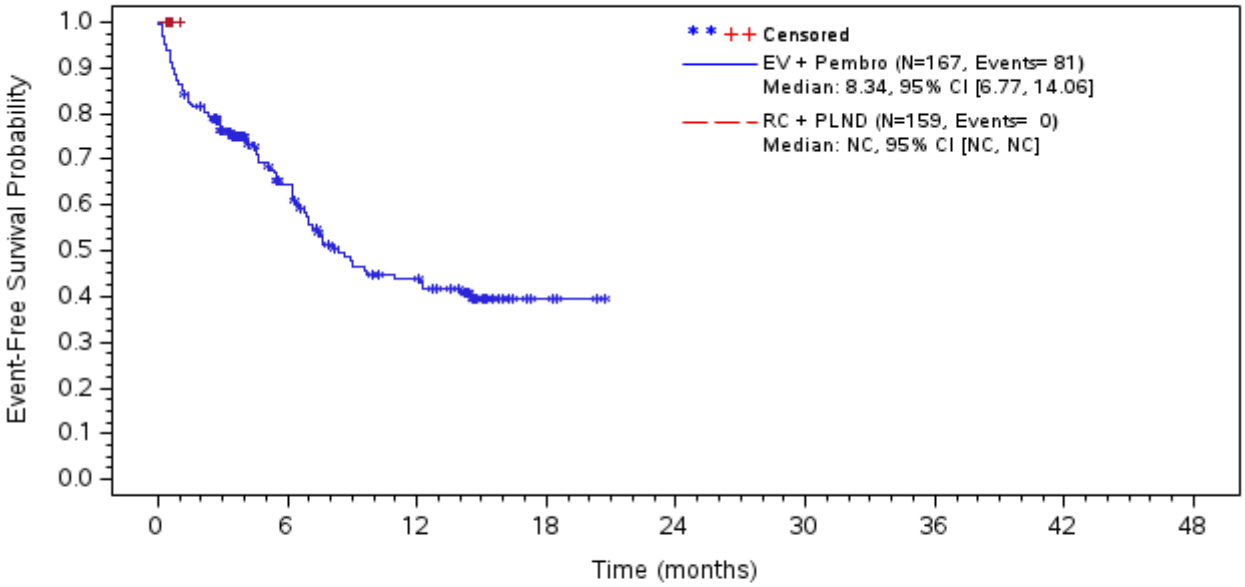
1	167 (0.0)	59 (15.0)	36 (22.8)	2 (40.1)	0 (41.3)	0 (41.3)	0 (41.3)	0 (41.3)	0 (41.3)
3	159 (0.0)	0 (59.1)	0 (59.1)	0 (59.1)	0 (59.1)	0 (59.1)	0 (59.1)	0 (59.1)	0 (59.1)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.4.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events leading to Treatment Discontinuation in Combined Treatment Phases - SAF2 Analysis Set



at Risk (% Censored)

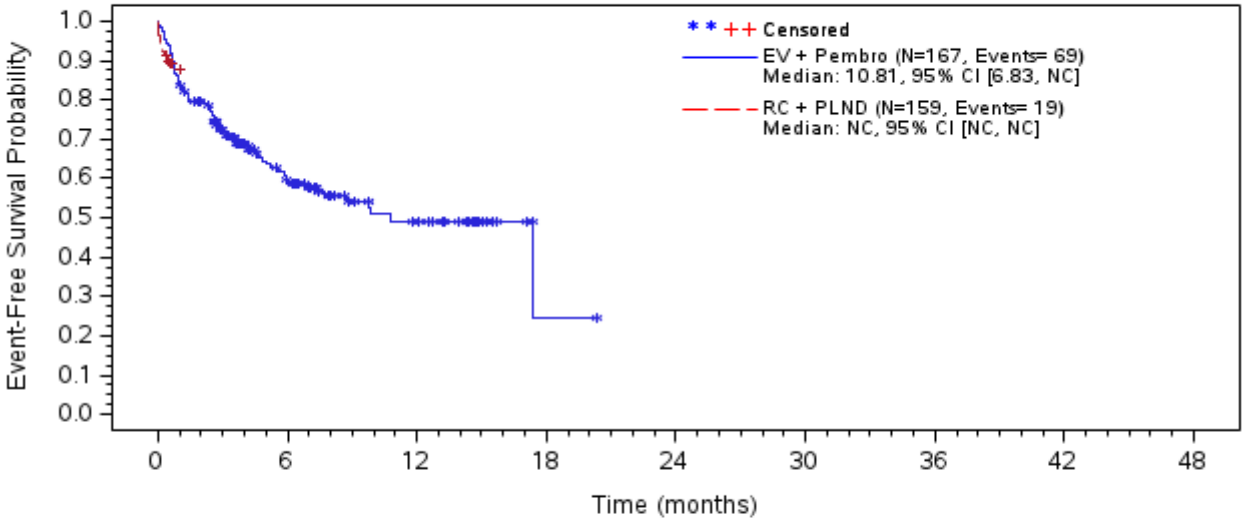
1	167 (0.0)	76 (22.2)	45 (26.9)	4 (49.1)	0 (51.5)	0 (51.5)	0 (51.5)	0 (51.5)	0 (51.5)
3	159 (0.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.5.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Blood and Lymphatic System Disorders (SOC) - SAF2 Analysis Set



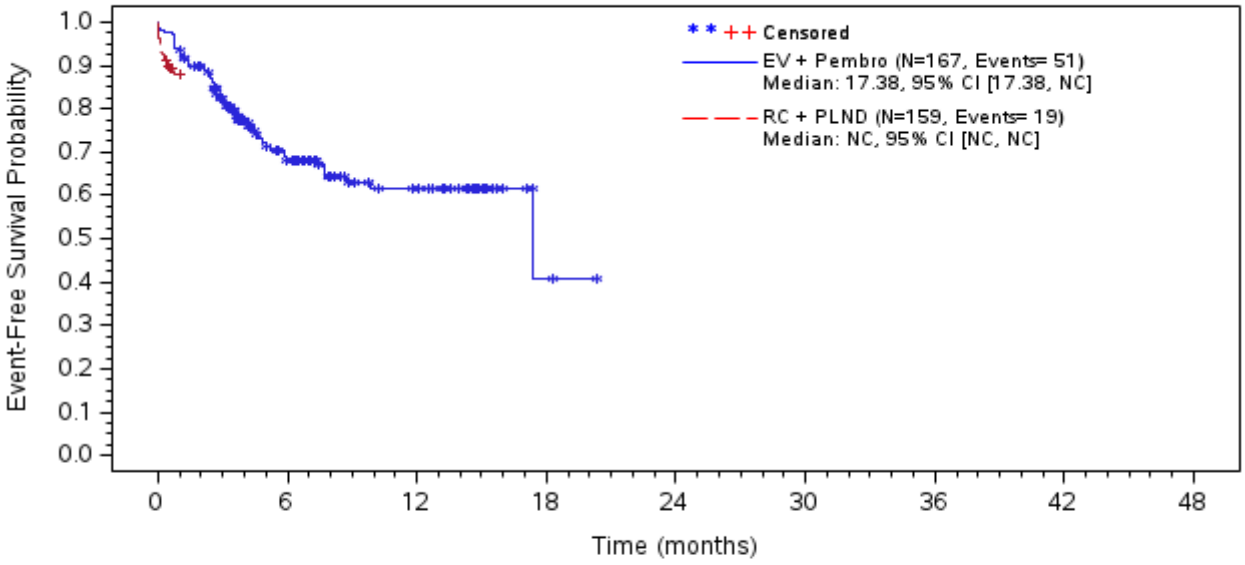
	# at Risk (% Censored)								
1	167 (0.0)	63 (26.3)	29 (41.9)	1 (58.1)	0 (58.7)	0 (58.7)	0 (58.7)	0 (58.7)	0 (58.7)
3	159 (0.0)	0 (88.1)	0 (88.1)	0 (88.1)	0 (88.1)	0 (88.1)	0 (88.1)	0 (88.1)	0 (88.1)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.6.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Anaemia (PT) - SAF2 Analysis Set



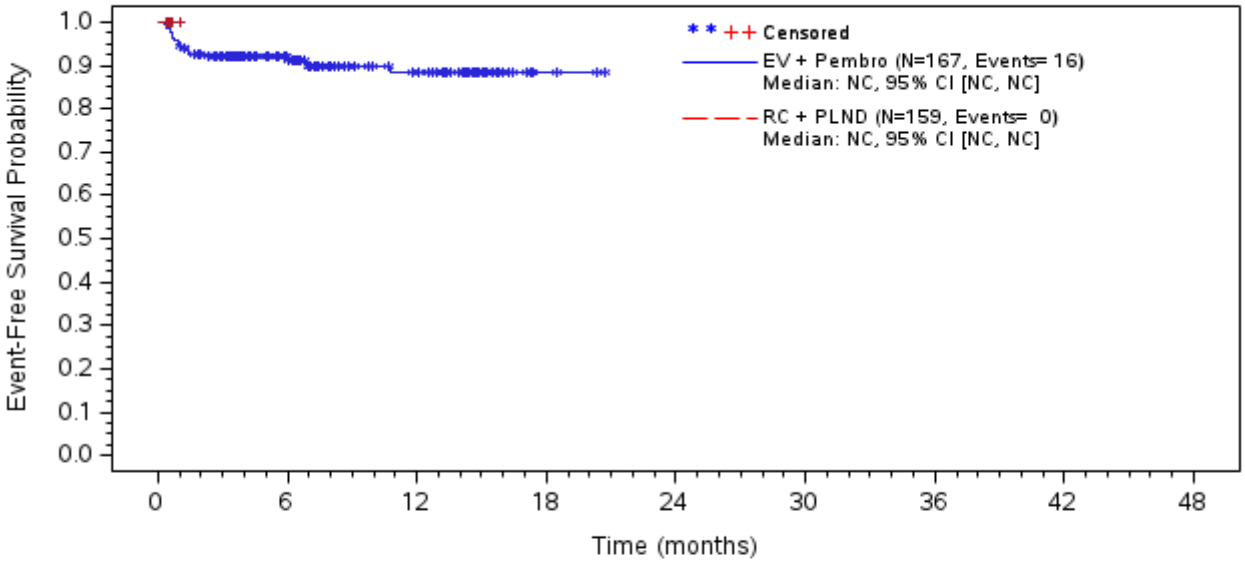
	# at Risk (% Censored)								
1	167 (0.0)	69 (31.7)	35 (49.1)	2 (68.3)	0 (69.5)	0 (69.5)	0 (69.5)	0 (69.5)	0 (69.5)
3	159 (0.0)	0 (88.1)	0 (88.1)	0 (88.1)	0 (88.1)	0 (88.1)	0 (88.1)	0 (88.1)	0 (88.1)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.7.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Neutropenia (PT) - SAF2 Analysis Set



at Risk (% Censored)

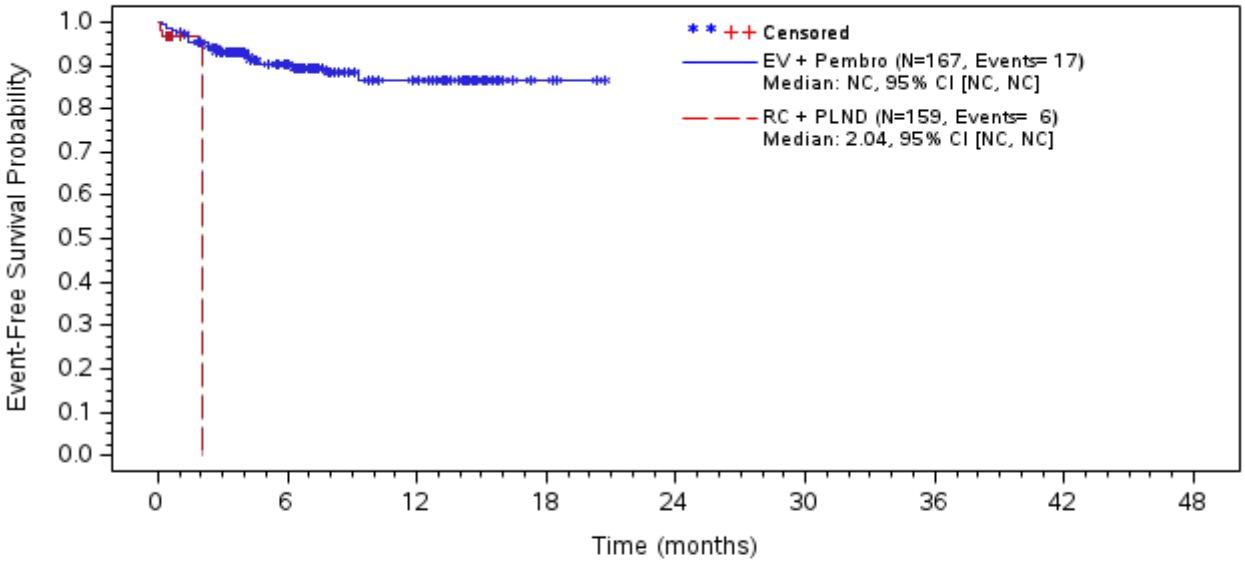
1	167 (0.0)	92 (37.1)	54 (58.1)	3 (88.6)	0 (90.4)	0 (90.4)	0 (90.4)	0 (90.4)	0 (90.4)
3	159 (0.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.8.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Cardiac Disorders (SOC) - SAF2 Analysis Set



at Risk (% Censored)

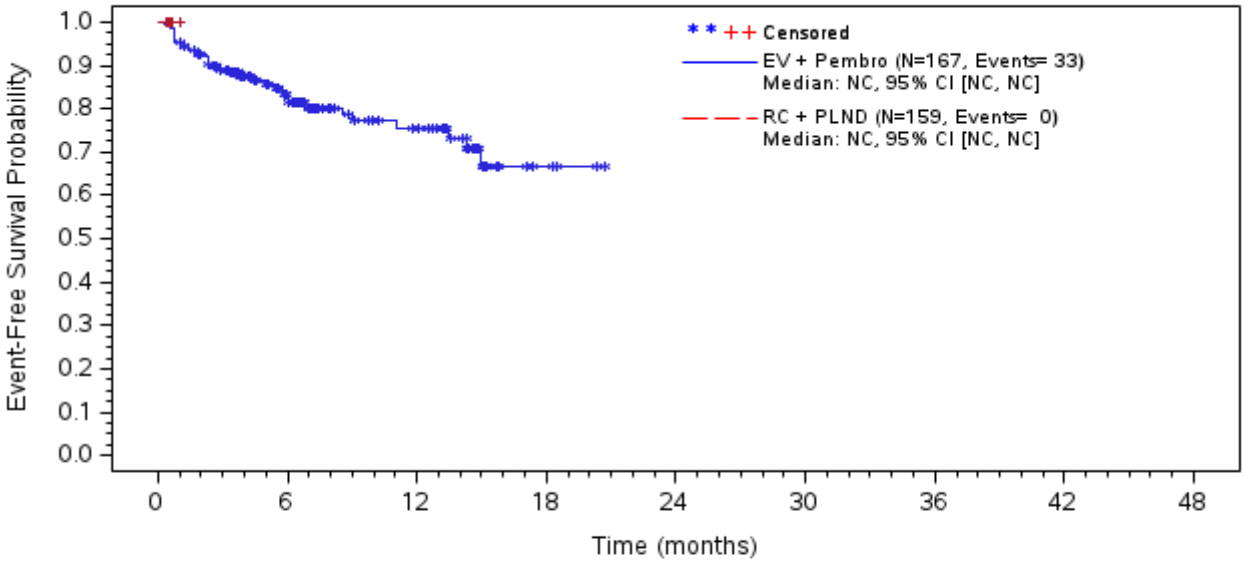
1	167 (0.0)	92 (36.5)	54 (57.5)	4 (87.4)	0 (89.8)	0 (89.8)	0 (89.8)	0 (89.8)	0 (89.8)
3	159 (0.0)	0 (96.2)	0 (96.2)	0 (96.2)	0 (96.2)	0 (96.2)	0 (96.2)	0 (96.2)	0 (96.2)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.9.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Endocrine Disorders (SOC) - SAF2 Analysis Set



at Risk (% Censored)

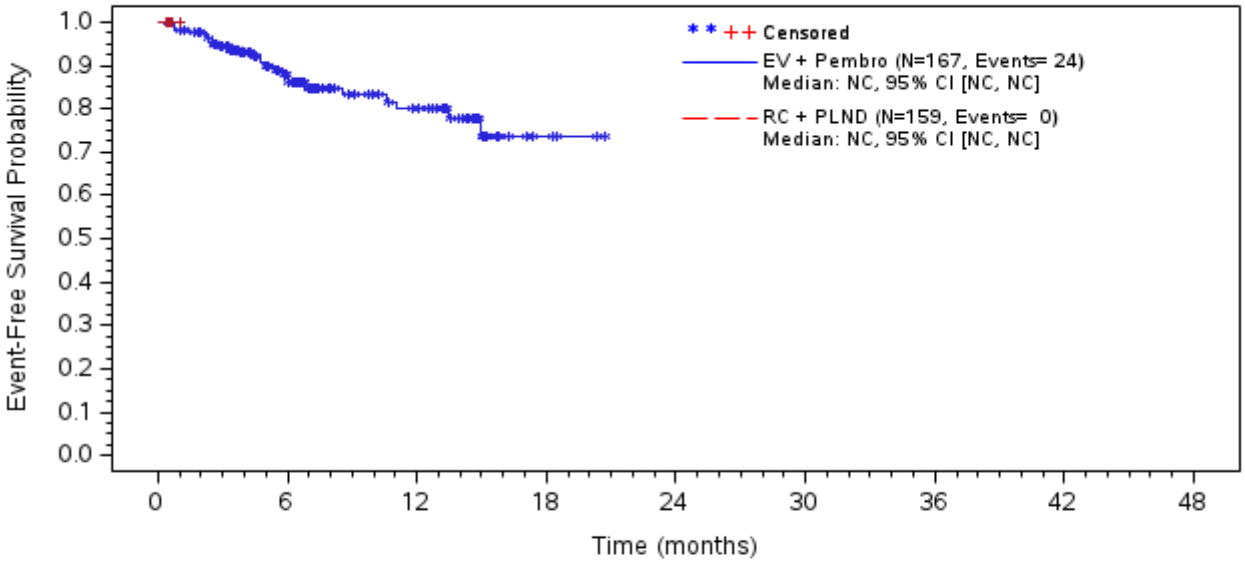
1	167 (0.0)	81 (37.1)	43 (56.3)	4 (77.8)	0 (80.2)	0 (80.2)	0 (80.2)	0 (80.2)	0 (80.2)
3	159 (0.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.10.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Hypothyroidism (PT) - SAF2 Analysis Set



at Risk (% Censored)

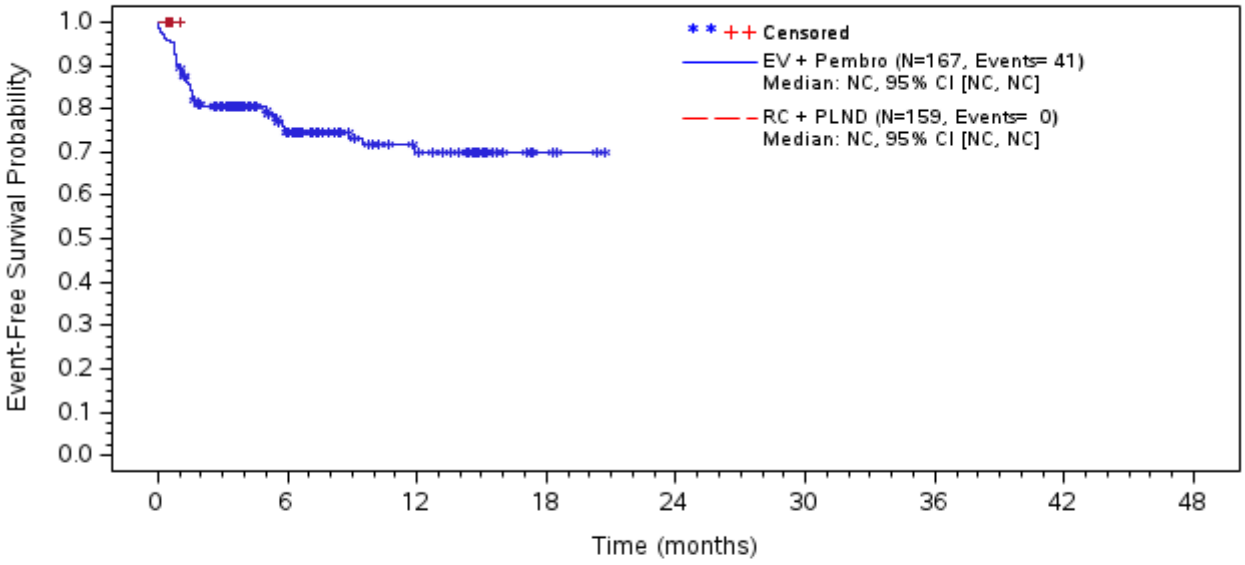
1	167 (0.0)	85 (39.5)	46 (59.3)	4 (83.2)	0 (85.6)	0 (85.6)	0 (85.6)	0 (85.6)	0 (85.6)
3	159 (0.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.11.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Eye Disorders (SOC) - SAF2 Analysis Set



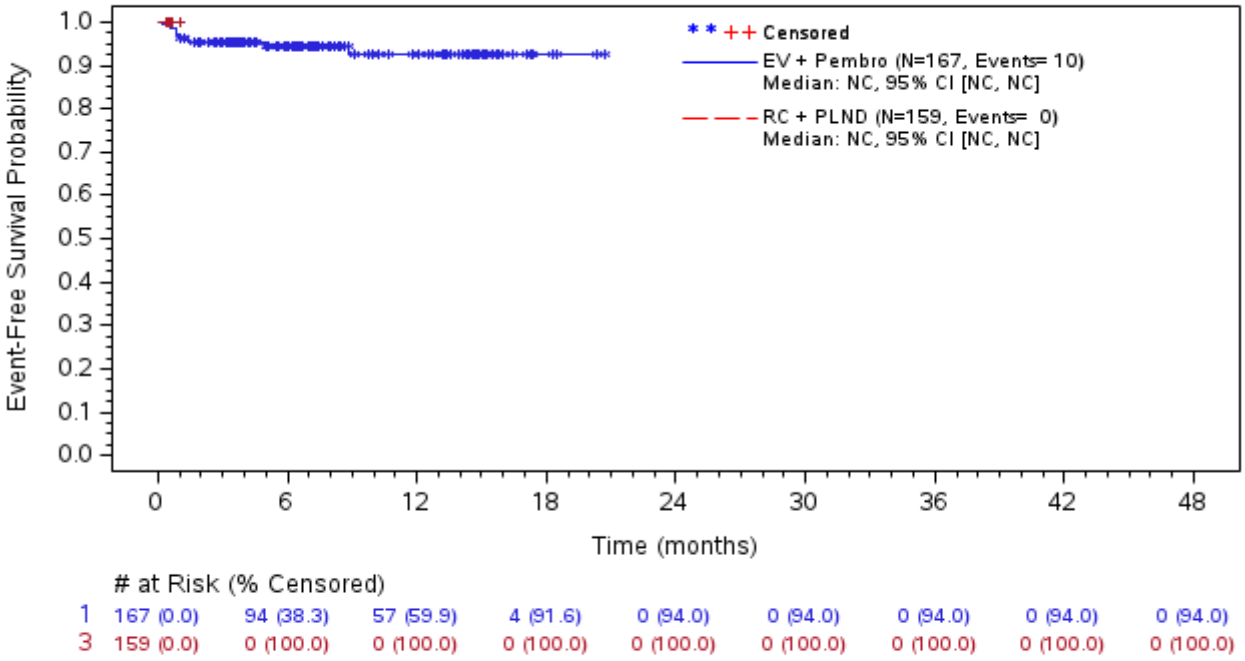
# at Risk (% Censored)									
1	167 (0.0)	73 (33.5)	40 (51.5)	4 (73.1)	0 (75.4)	0 (75.4)	0 (75.4)	0 (75.4)	0 (75.4)
3	159 (0.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.12.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Dry Eye (PT) - SAF2 Analysis Set



at Risk (% Censored)

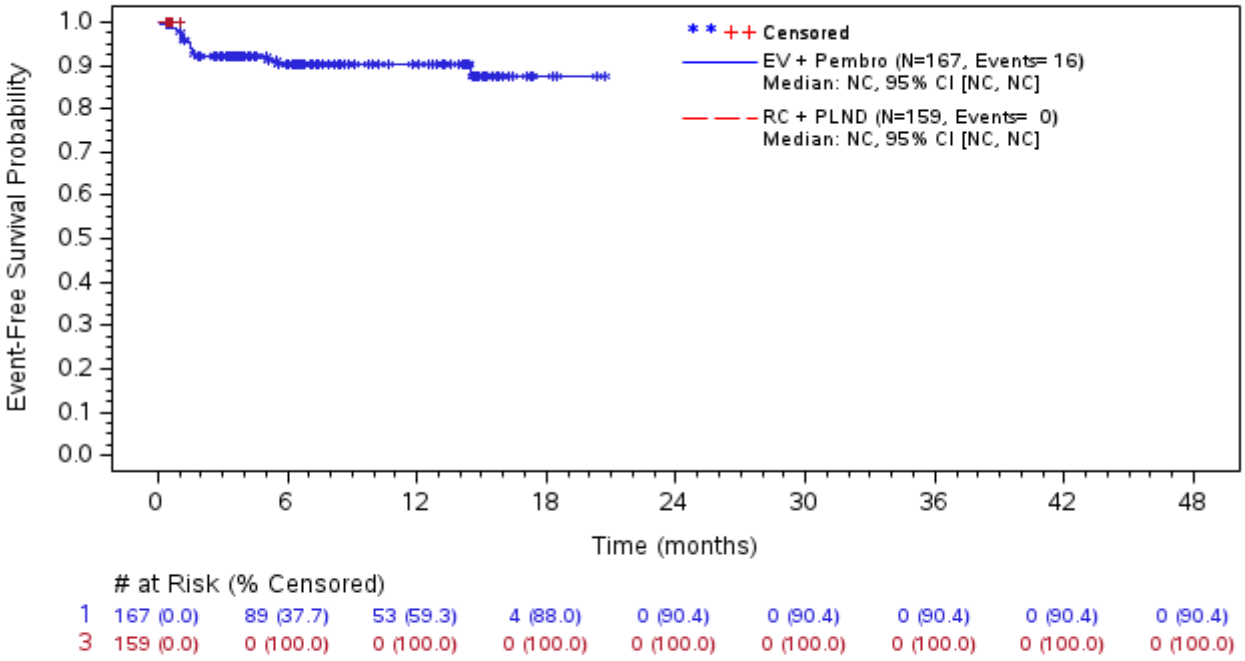
1	167 (0.0)	94 (38.3)	57 (59.9)	4 (91.6)	0 (94.0)	0 (94.0)	0 (94.0)	0 (94.0)	0 (94.0)
3	159 (0.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.13.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Lacrimation Increased (PT) - SAF2 Analysis Set



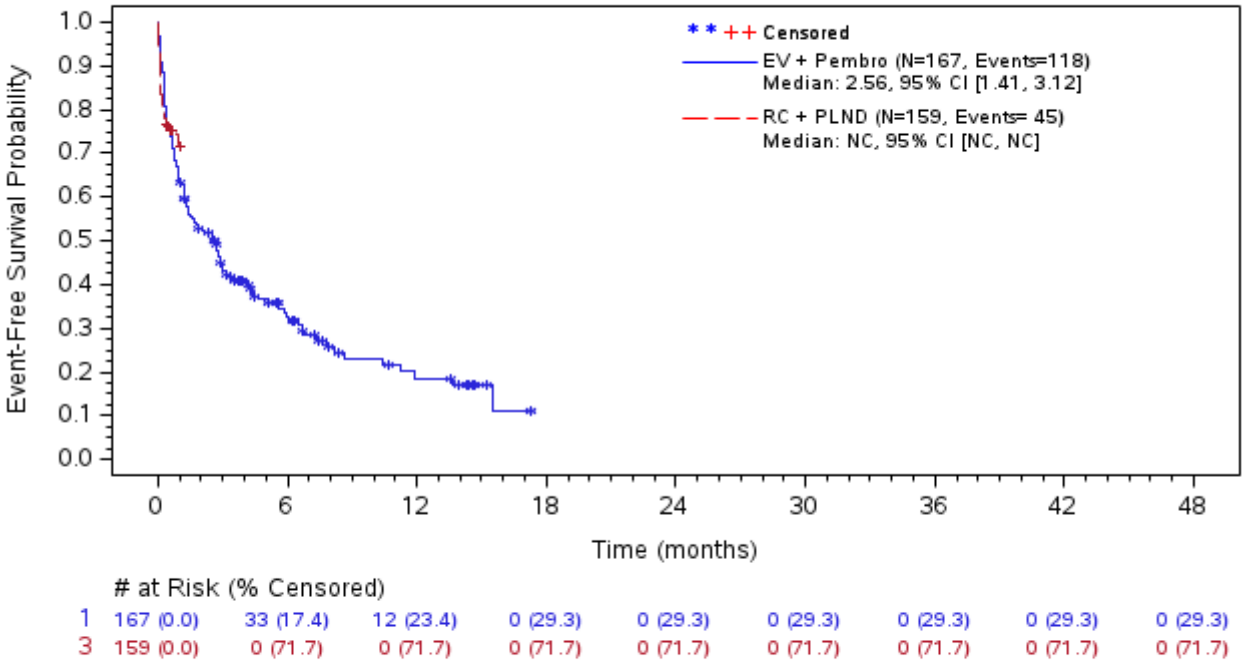
# at Risk (% Censored)									
1	167 (0.0)	89 (37.7)	53 (59.3)	4 (88.0)	0 (90.4)	0 (90.4)	0 (90.4)	0 (90.4)	0 (90.4)
3	159 (0.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.14.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Gastrointestinal Disorders (SOC) - SAF2 Analysis Set



at Risk (% Censored)

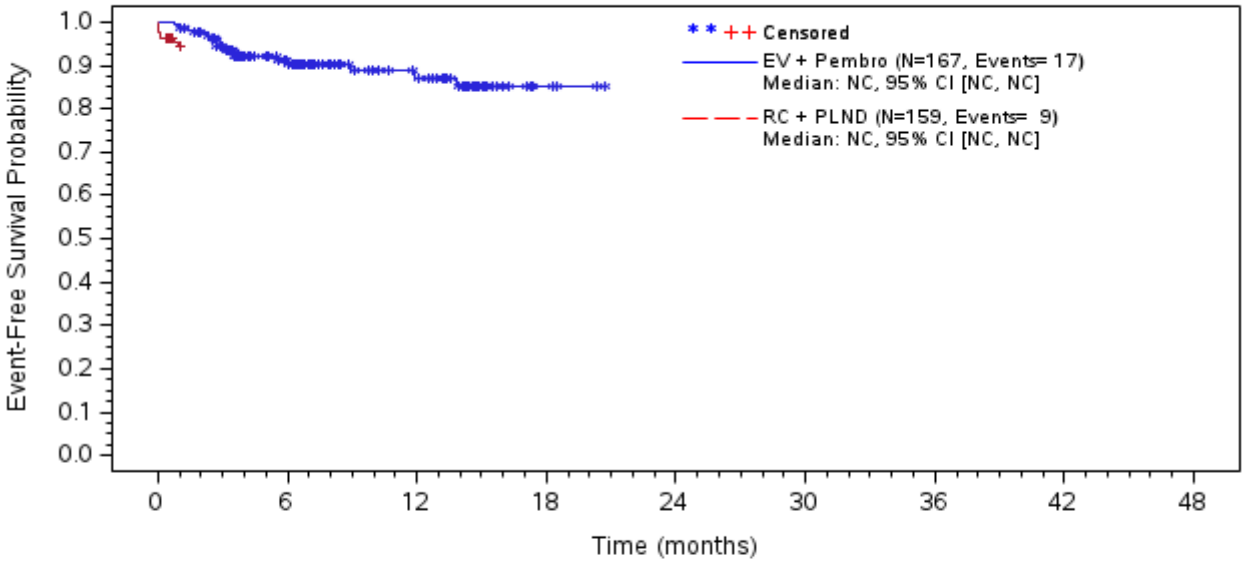
1	167 (0.0)	33 (17.4)	12 (23.4)	0 (29.3)	0 (29.3)	0 (29.3)	0 (29.3)	0 (29.3)	0 (29.3)
3	159 (0.0)	0 (71.7)	0 (71.7)	0 (71.7)	0 (71.7)	0 (71.7)	0 (71.7)	0 (71.7)	0 (71.7)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.15.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Abdominal Pain (PT) - SAF2 Analysis Set



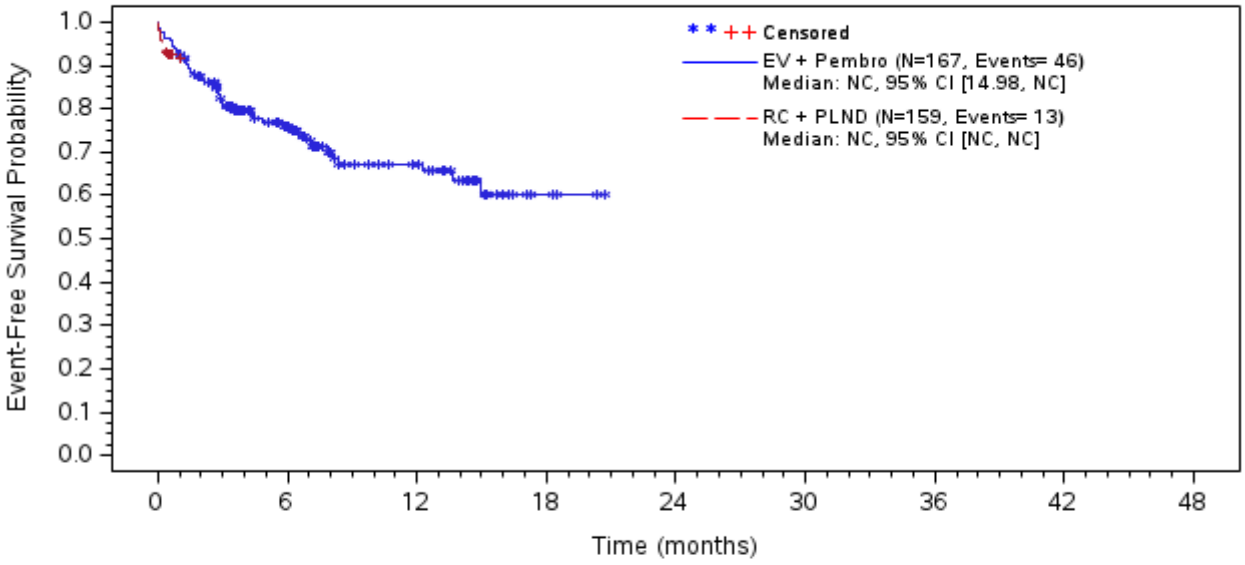
	# at Risk (% Censored)								
1	167 (0.0)	91 (37.7)	53 (58.7)	4 (87.4)	0 (89.8)	0 (89.8)	0 (89.8)	0 (89.8)	0 (89.8)
3	159 (0.0)	0 (94.3)	0 (94.3)	0 (94.3)	0 (94.3)	0 (94.3)	0 (94.3)	0 (94.3)	0 (94.3)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.16.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Constipation (PT) - SAF2 Analysis Set



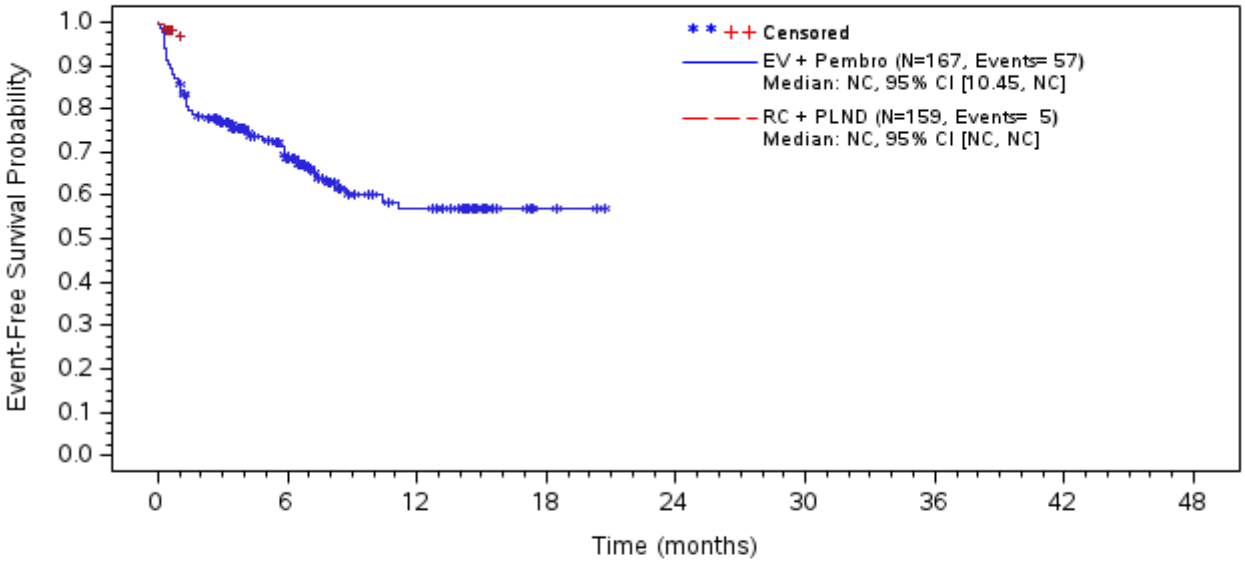
	# at Risk (% Censored)								
1	167 (0.0)	73 (34.7)	41 (49.7)	4 (70.1)	0 (72.5)	0 (72.5)	0 (72.5)	0 (72.5)	0 (72.5)
3	159 (0.0)	0 (91.8)	0 (91.8)	0 (91.8)	0 (91.8)	0 (91.8)	0 (91.8)	0 (91.8)	0 (91.8)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.17.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Diarrhoea (PT) - SAF2 Analysis Set



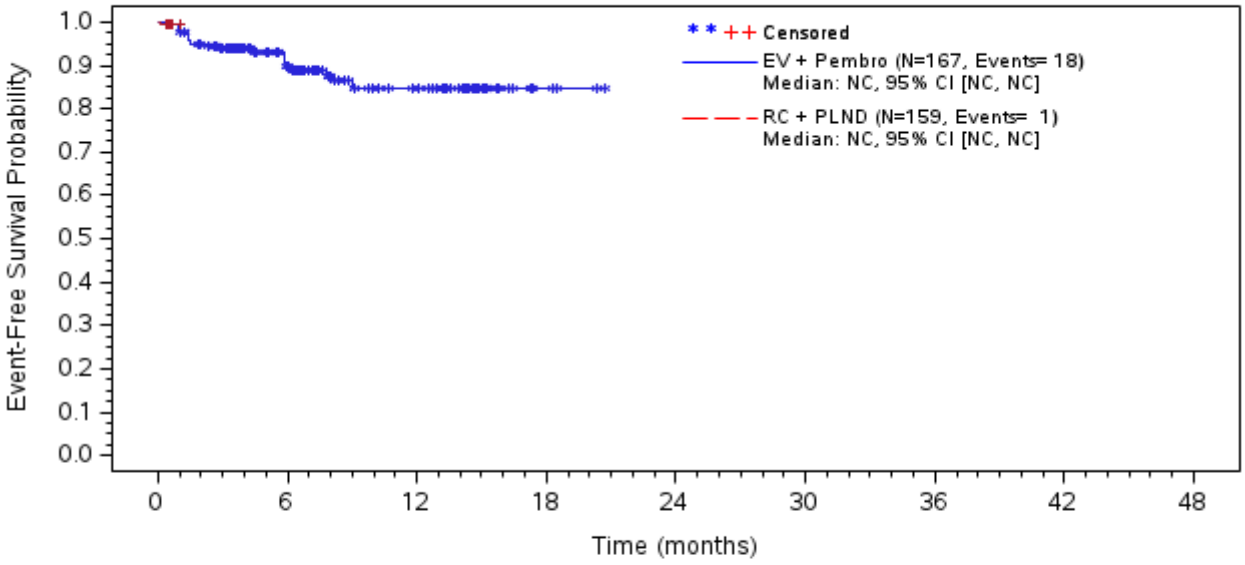
# at Risk (% Censored)									
1	167 (0.0)	72 (28.1)	35 (44.9)	3 (64.1)	0 (65.9)	0 (65.9)	0 (65.9)	0 (65.9)	0 (65.9)
3	159 (0.0)	0 (96.9)	0 (96.9)	0 (96.9)	0 (96.9)	0 (96.9)	0 (96.9)	0 (96.9)	0 (96.9)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.18.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Dry Mouth (PT) - SAF2 Analysis Set



at Risk (% Censored)

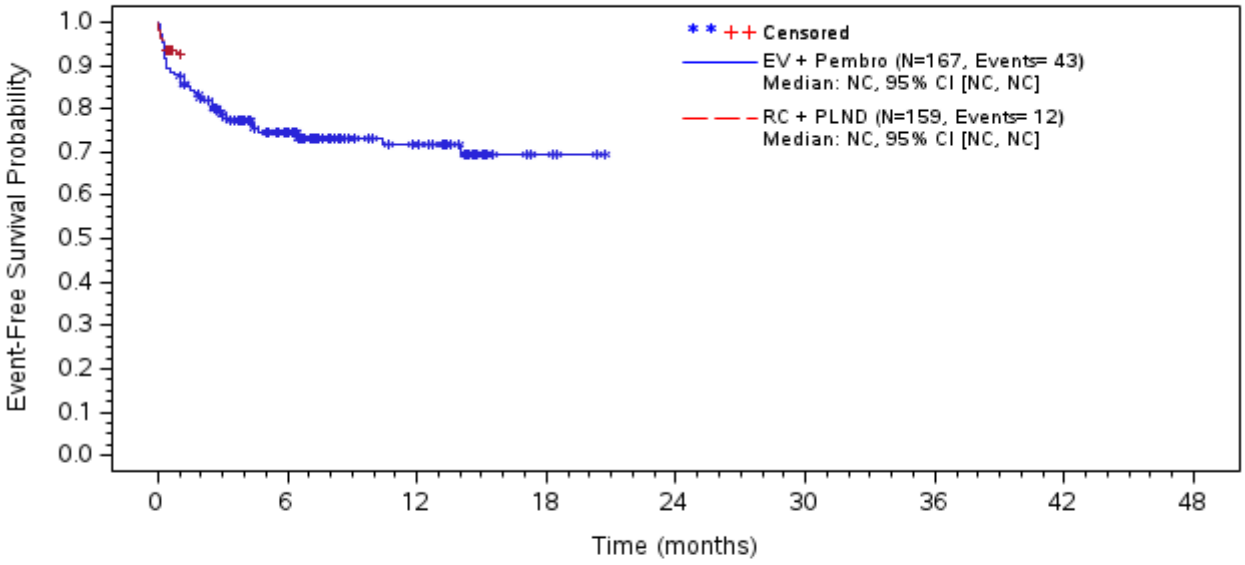
1	167 (0.0)	90 (37.7)	52 (58.1)	4 (86.8)	0 (89.2)	0 (89.2)	0 (89.2)	0 (89.2)	0 (89.2)
3	159 (0.0)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.19.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Nausea (PT) - SAF2 Analysis Set



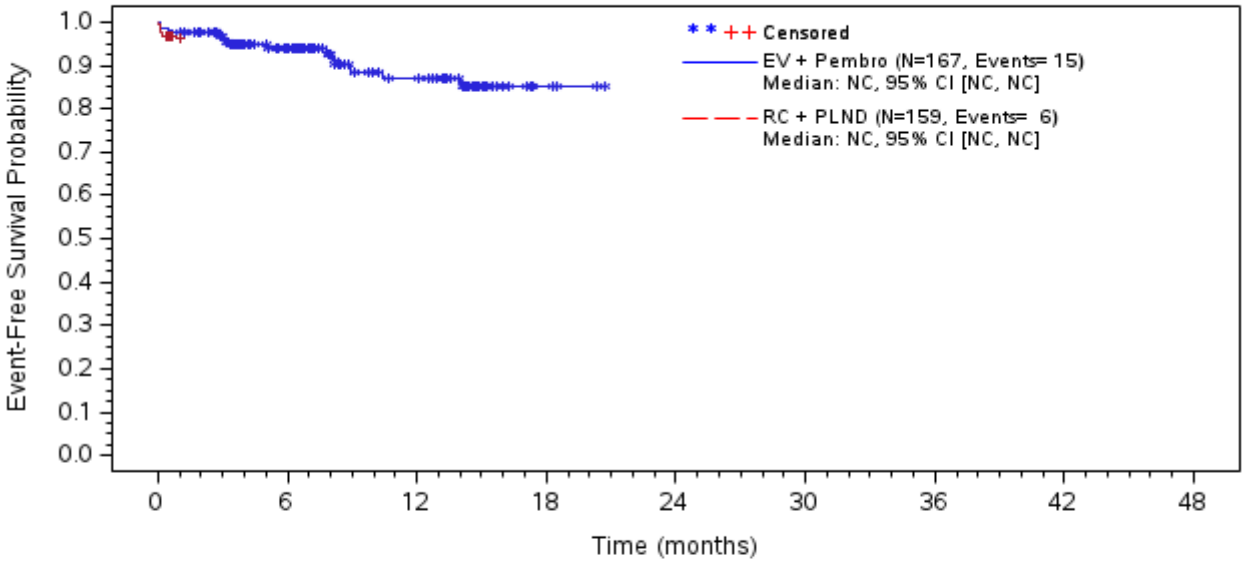
	# at Risk (% Censored)								
1	167 (0.0)	74 (31.7)	40 (50.9)	4 (71.9)	0 (74.3)	0 (74.3)	0 (74.3)	0 (74.3)	0 (74.3)
3	159 (0.0)	0 (92.5)	0 (92.5)	0 (92.5)	0 (92.5)	0 (92.5)	0 (92.5)	0 (92.5)	0 (92.5)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.20.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Vomiting (PT) - SAF2 Analysis Set



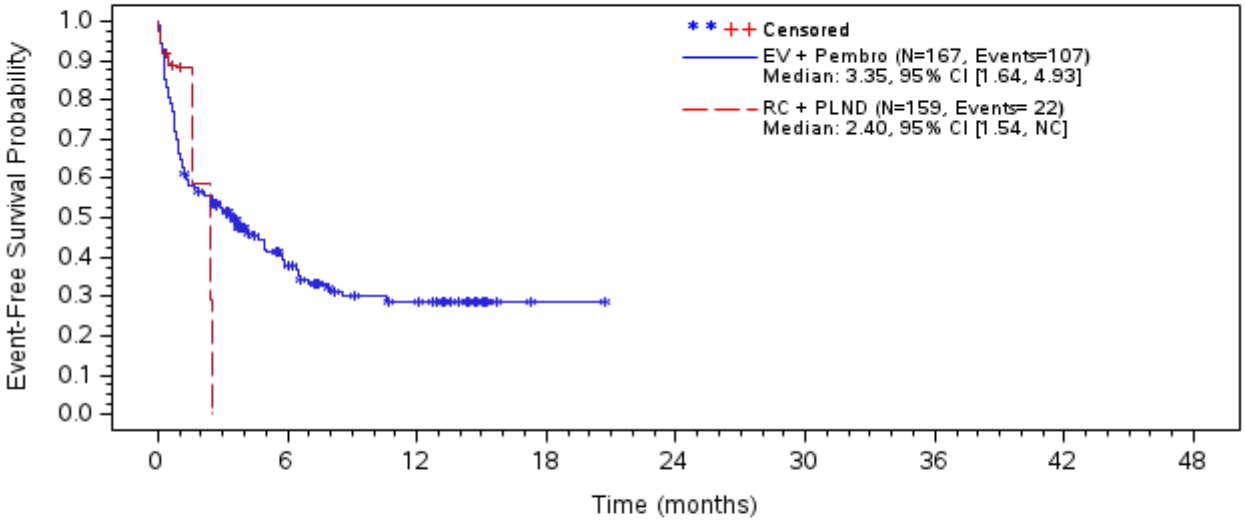
# at Risk (% Censored)									
1	167 (0.0)	94 (38.3)	54 (59.3)	4 (88.6)	0 (91.0)	0 (91.0)	0 (91.0)	0 (91.0)	0 (91.0)
3	159 (0.0)	0 (96.2)	0 (96.2)	0 (96.2)	0 (96.2)	0 (96.2)	0 (96.2)	0 (96.2)	0 (96.2)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.21.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - General Disorders and Administration Site Conditions (SOC) - SAF2 Analysis Set



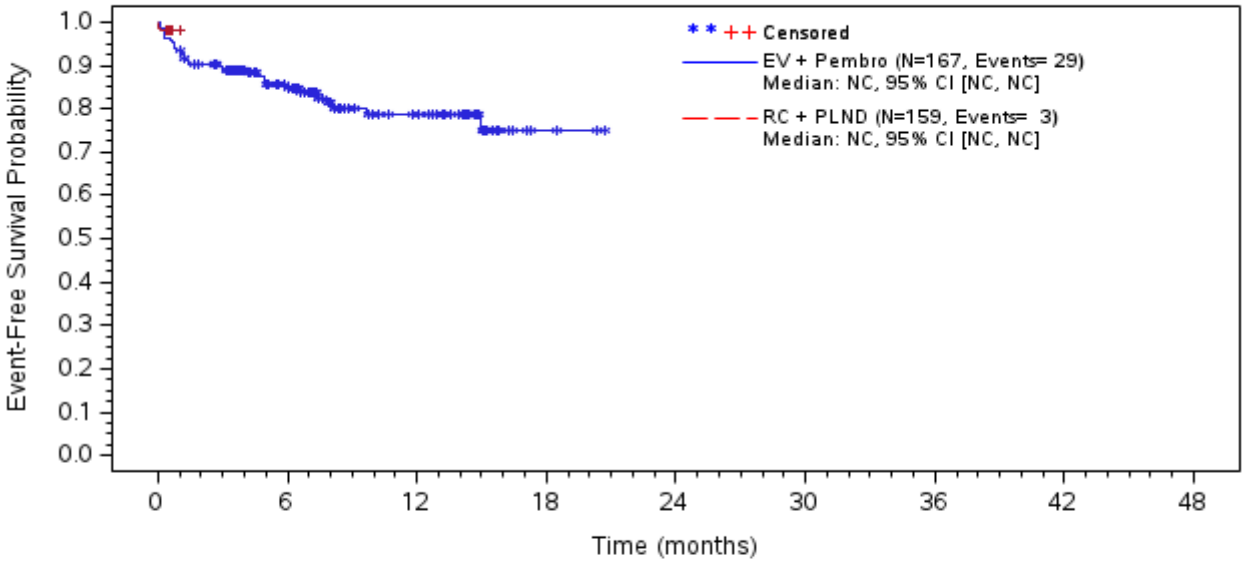
# at Risk (% Censored)									
1	167 (0.0)	44 (15.0)	24 (21.6)	1 (35.3)	0 (35.9)	0 (35.9)	0 (35.9)	0 (35.9)	0 (35.9)
3	159 (0.0)	0 (86.2)	0 (86.2)	0 (86.2)	0 (86.2)	0 (86.2)	0 (86.2)	0 (86.2)	0 (86.2)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.22.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Asthenia (PT) - SAF2 Analysis Set



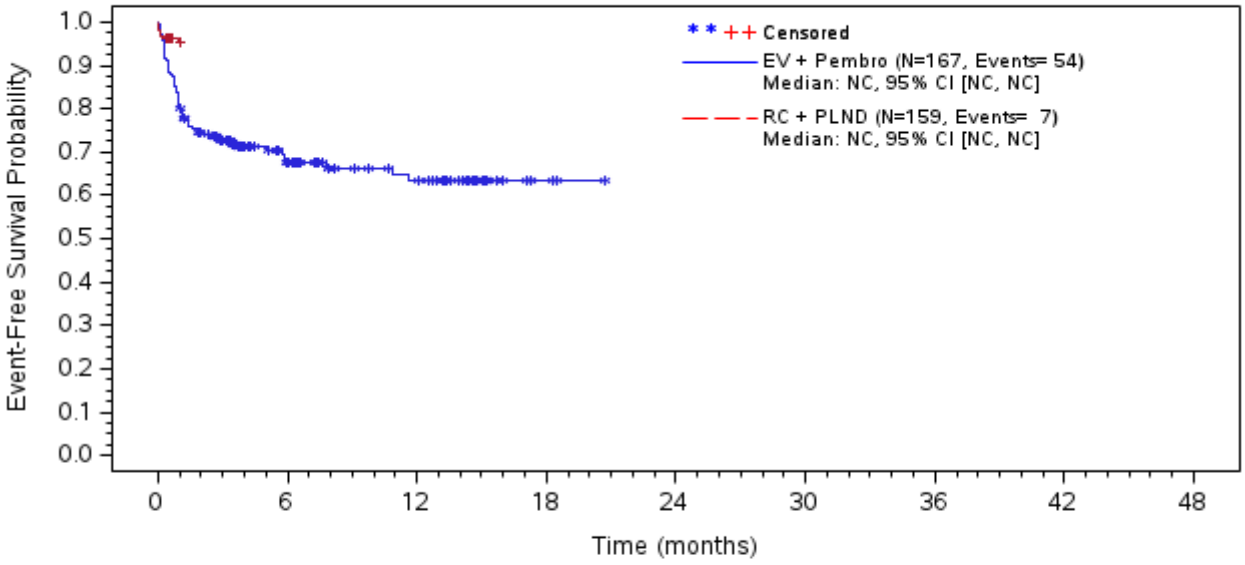
# at Risk (% Censored)									
1	167 (0.0)	90 (32.3)	48 (54.5)	3 (80.8)	0 (82.6)	0 (82.6)	0 (82.6)	0 (82.6)	0 (82.6)
3	159 (0.0)	0 (98.1)	0 (98.1)	0 (98.1)	0 (98.1)	0 (98.1)	0 (98.1)	0 (98.1)	0 (98.1)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.23.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Fatigue (PT) - SAF2 Analysis Set



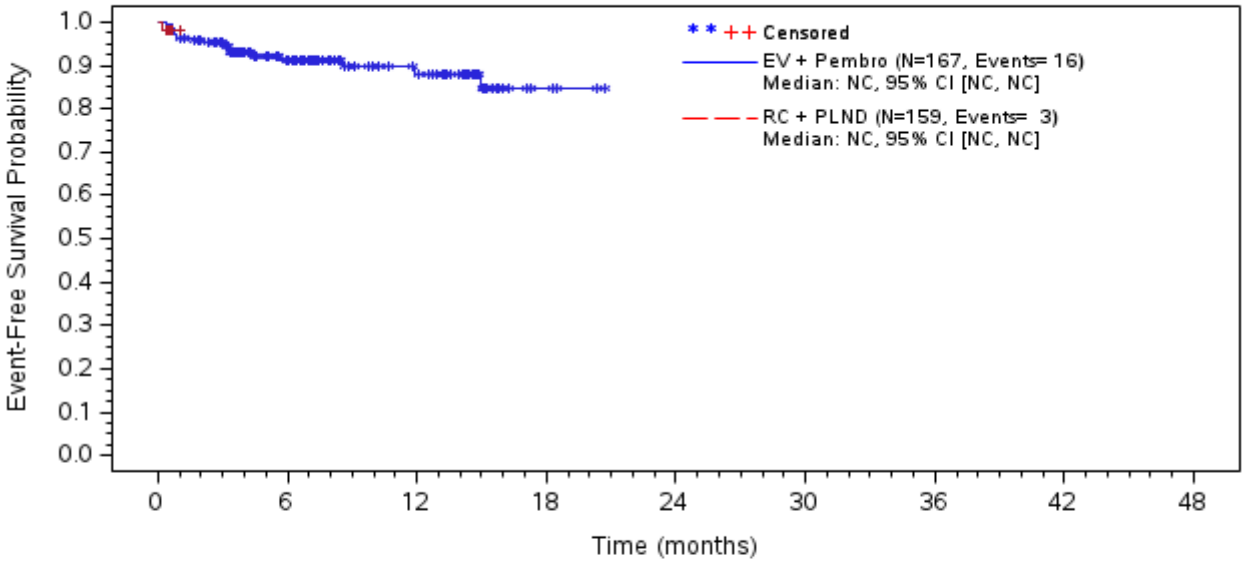
	# at Risk (% Censored)								
1	167 (0.0)	69 (28.1)	46 (40.1)	3 (65.9)	0 (67.7)	0 (67.7)	0 (67.7)	0 (67.7)	0 (67.7)
3	159 (0.0)	0 (95.6)	0 (95.6)	0 (95.6)	0 (95.6)	0 (95.6)	0 (95.6)	0 (95.6)	0 (95.6)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.24.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Oedema Peripheral (PT) - SAF2 Analysis Set



at Risk (% Censored)

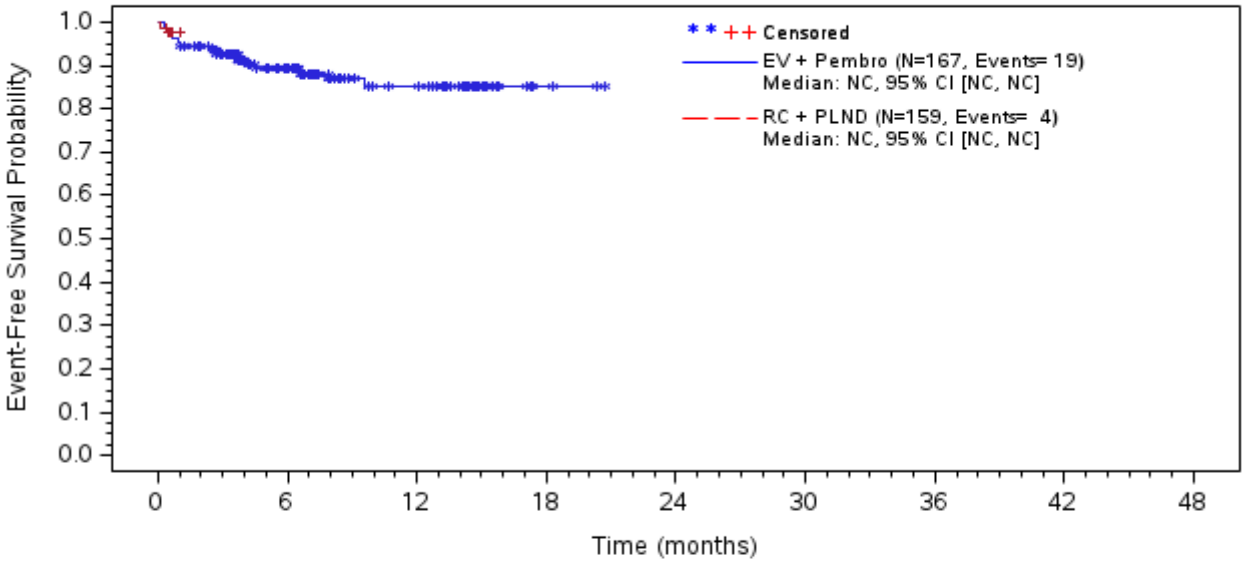
1	167 (0.0)	90 (38.3)	53 (59.3)	4 (88.0)	0 (90.4)	0 (90.4)	0 (90.4)	0 (90.4)	0 (90.4)
3	159 (0.0)	0 (98.1)	0 (98.1)	0 (98.1)	0 (98.1)	0 (98.1)	0 (98.1)	0 (98.1)	0 (98.1)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.25.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Pyrexia (PT) - SAF2 Analysis Set



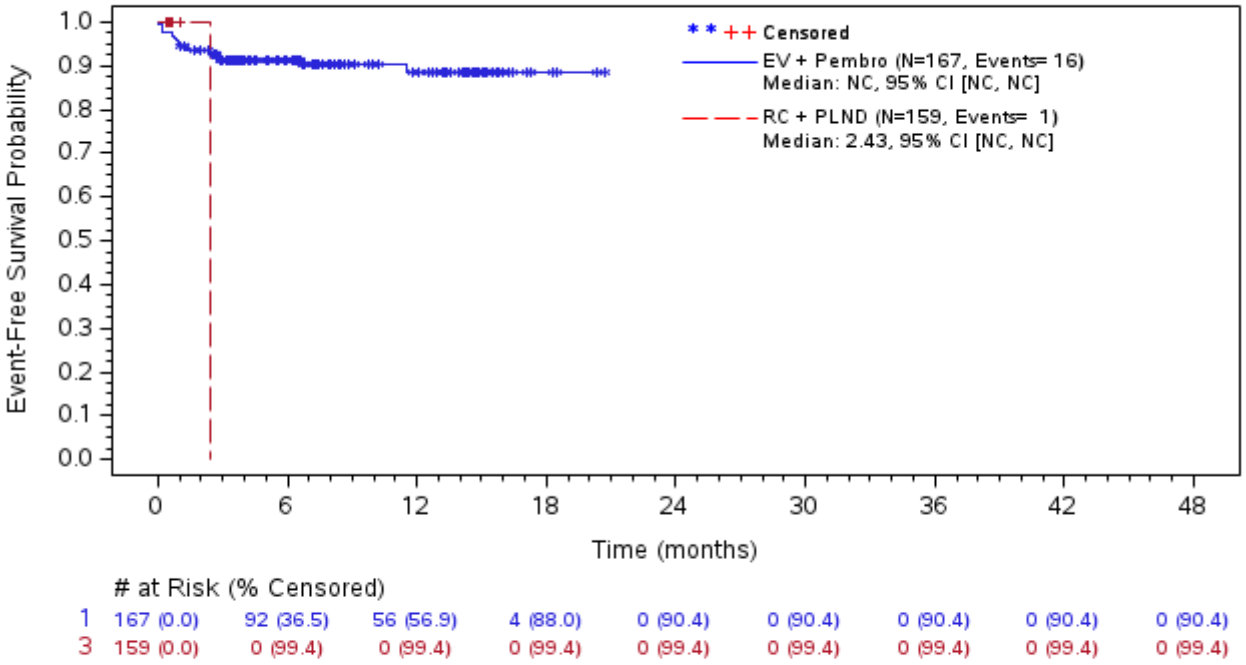
# at Risk (% Censored)									
1	167 (0.0)	86 (38.9)	48 (59.9)	3 (86.8)	0 (88.6)	0 (88.6)	0 (88.6)	0 (88.6)	0 (88.6)
3	159 (0.0)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.26.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Hepatobiliary Disorders (SOC) - SAF2 Analysis Set



at Risk (% Censored)

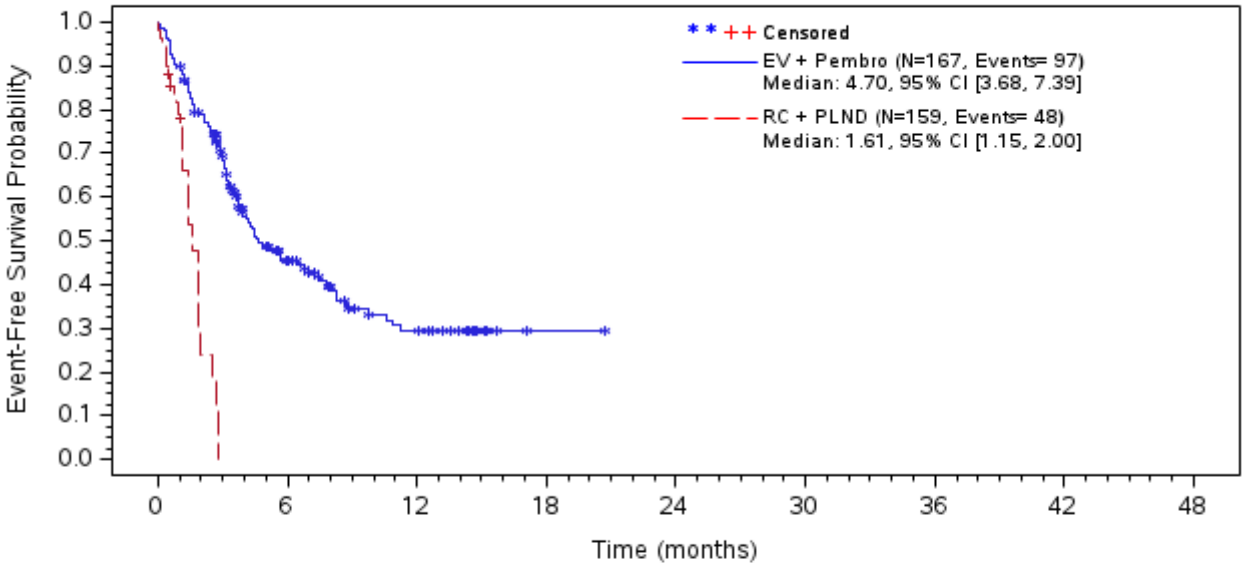
1	167 (0.0)	92 (36.5)	56 (56.9)	4 (88.0)	0 (90.4)	0 (90.4)	0 (90.4)	0 (90.4)	0 (90.4)
3	159 (0.0)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.27.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Infections and Infestations (SOC) - SAF2 Analysis Set



at Risk (% Censored)

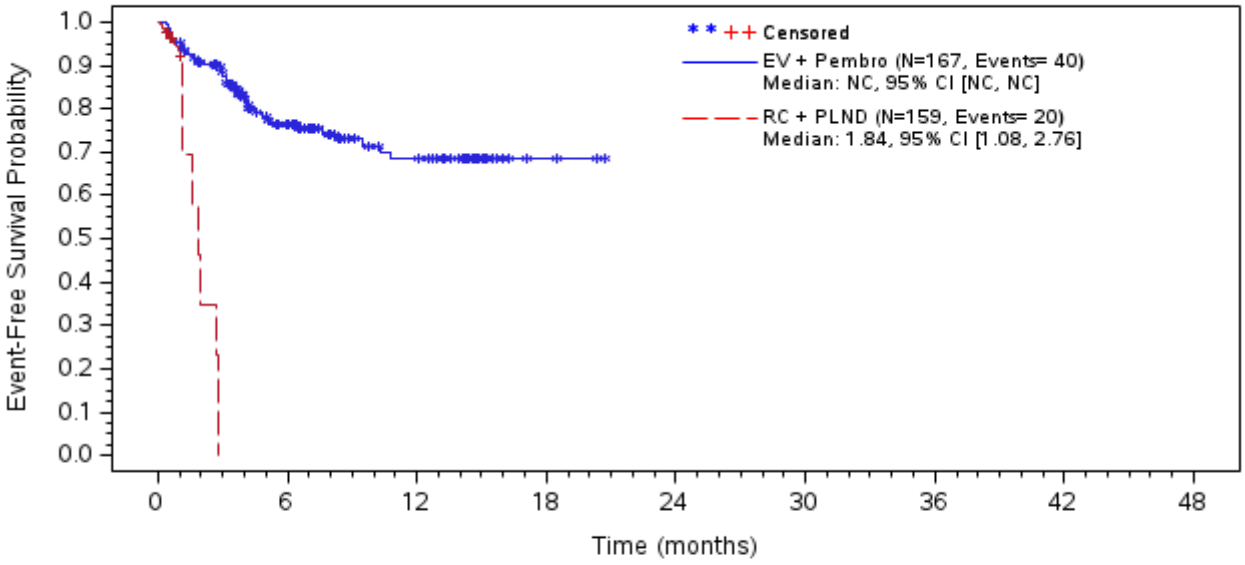
1	167 (0.0)	53 (19.2)	24 (27.5)	1 (41.3)	0 (41.9)	0 (41.9)	0 (41.9)	0 (41.9)	0 (41.9)
3	159 (0.0)	0 (69.8)	0 (69.8)	0 (69.8)	0 (69.8)	0 (69.8)	0 (69.8)	0 (69.8)	0 (69.8)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.28.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Urinary Tract Infection (PT) - SAF2 Analysis Set



at Risk (% Censored)

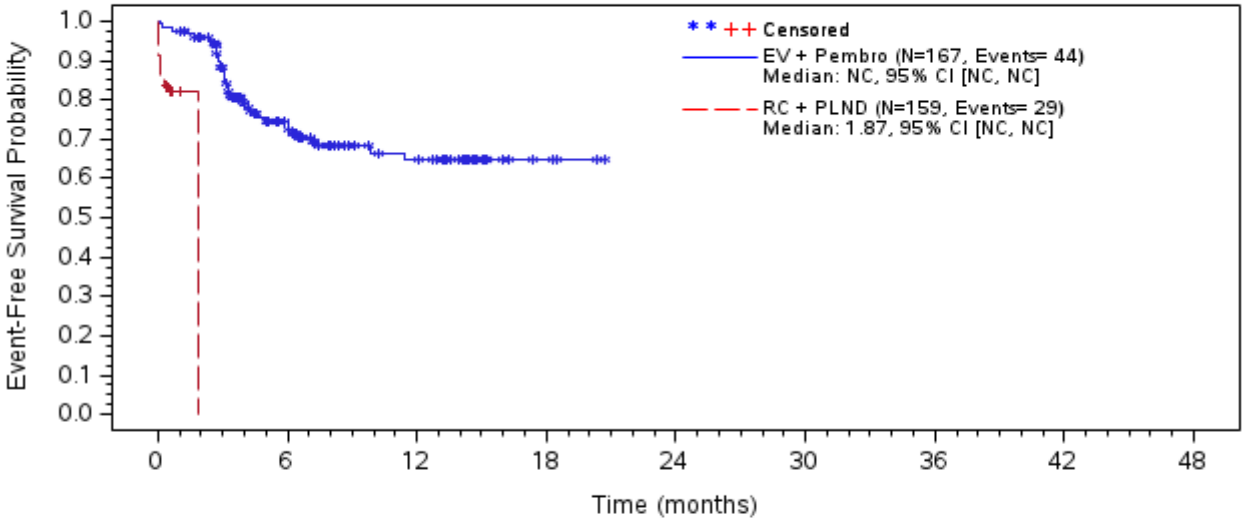
1	167 (0.0)	79 (32.3)	45 (49.1)	3 (74.3)	0 (76.0)	0 (76.0)	0 (76.0)	0 (76.0)	0 (76.0)
3	159 (0.0)	0 (87.4)	0 (87.4)	0 (87.4)	0 (87.4)	0 (87.4)	0 (87.4)	0 (87.4)	0 (87.4)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.29.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Injury, Poisoning and Procedural Complications (SOC) - SAF2 Analysis Set



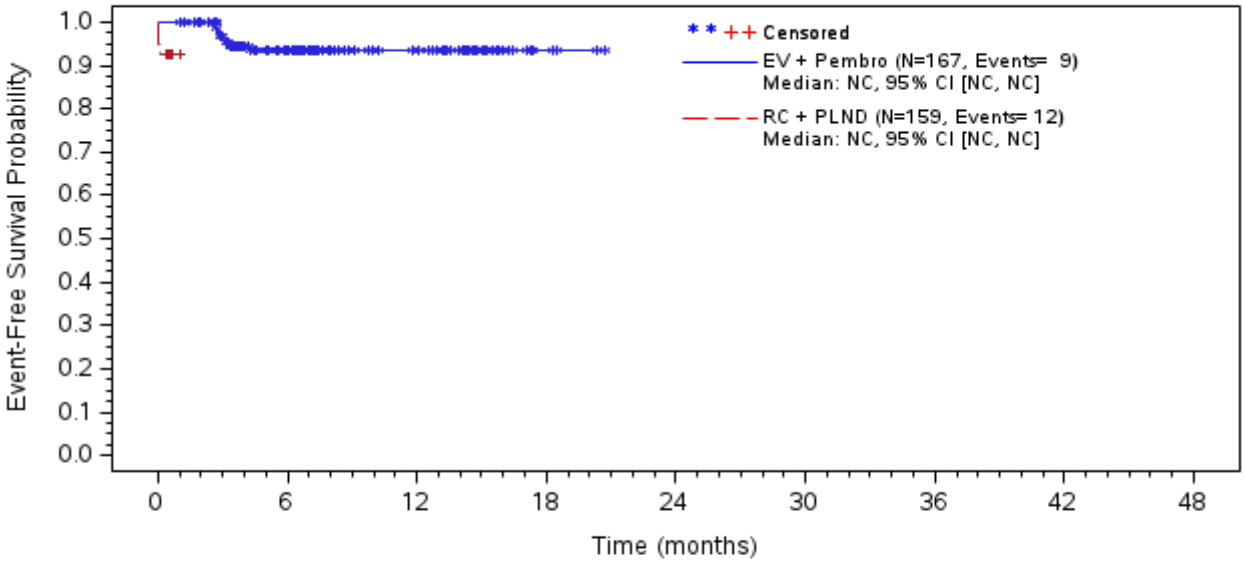
	# at Risk (% Censored)								
1	167 (0.0)	75 (33.5)	40 (49.7)	4 (71.3)	0 (73.7)	0 (73.7)	0 (73.7)	0 (73.7)	0 (73.7)
3	159 (0.0)	0 (81.8)	0 (81.8)	0 (81.8)	0 (81.8)	0 (81.8)	0 (81.8)	0 (81.8)	0 (81.8)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.30.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Procedural Pain (PT) - SAF2 Analysis Set



at Risk (% Censored)

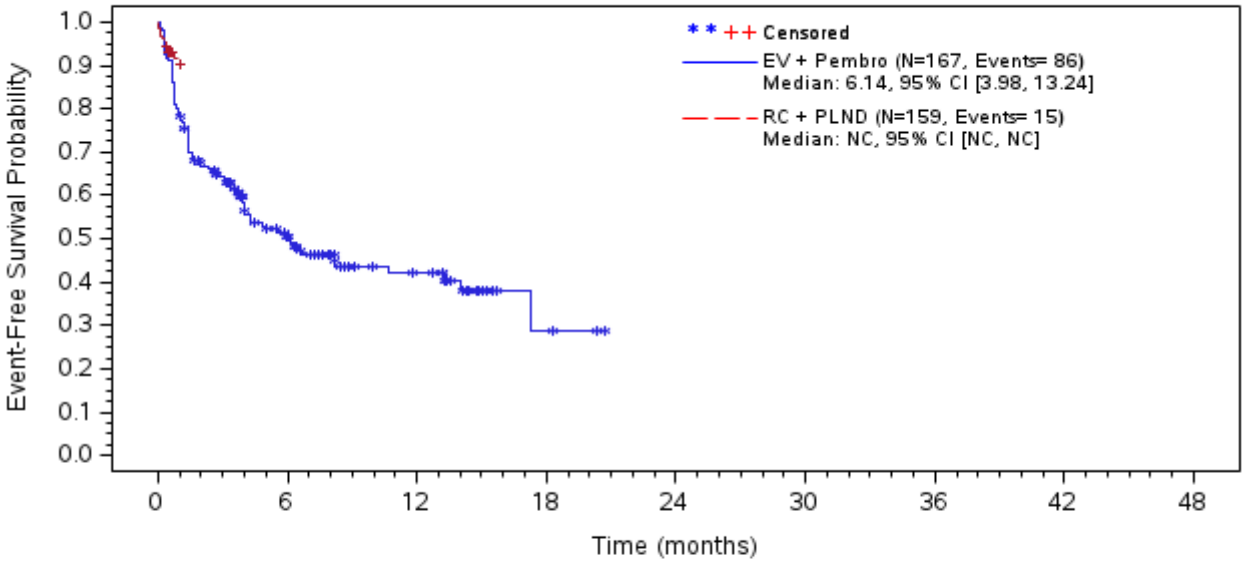
1	167 (0.0)	90 (40.7)	53 (62.9)	4 (92.2)	0 (94.6)	0 (94.6)	0 (94.6)	0 (94.6)	0 (94.6)
3	159 (0.0)	0 (92.5)	0 (92.5)	0 (92.5)	0 (92.5)	0 (92.5)	0 (92.5)	0 (92.5)	0 (92.5)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.31.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Investigations (SOC) - SAF2 Analysis Set



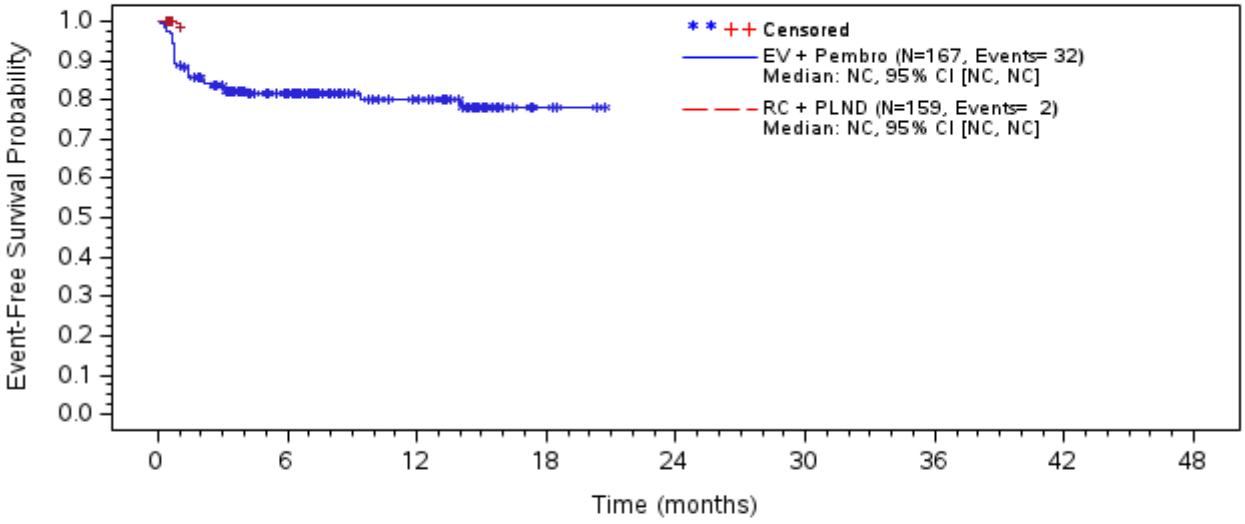
	# at Risk (% Censored)								
1	167 (0.0)	53 (22.8)	26 (34.7)	3 (46.7)	0 (48.5)	0 (48.5)	0 (48.5)	0 (48.5)	0 (48.5)
3	159 (0.0)	0 (90.6)	0 (90.6)	0 (90.6)	0 (90.6)	0 (90.6)	0 (90.6)	0 (90.6)	0 (90.6)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.32.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Alanine Aminotransferase Increased (PT) - SAF2 Analysis Set



at Risk (% Censored)

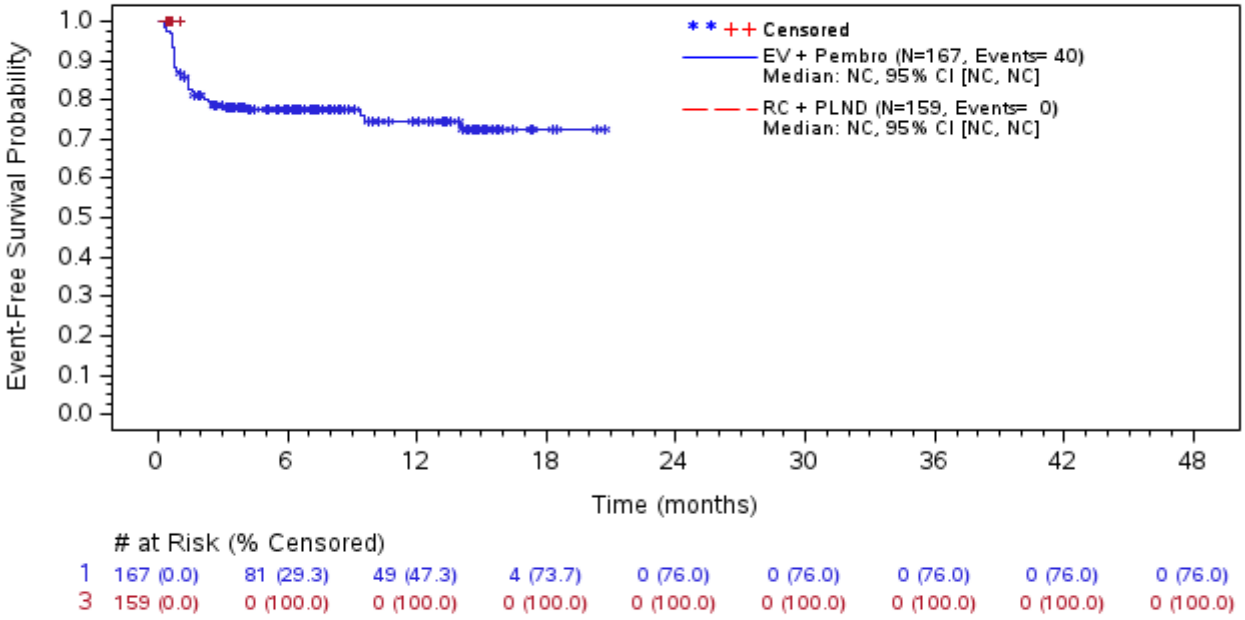
1	167 (0.0)	86 (30.5)	53 (49.7)	4 (78.4)	0 (80.8)	0 (80.8)	0 (80.8)	0 (80.8)	0 (80.8)
3	159 (0.0)	0 (98.7)	0 (98.7)	0 (98.7)	0 (98.7)	0 (98.7)	0 (98.7)	0 (98.7)	0 (98.7)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.33.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Aspartate Aminotransferase Increased (PT) - SAF2 Analysis Set



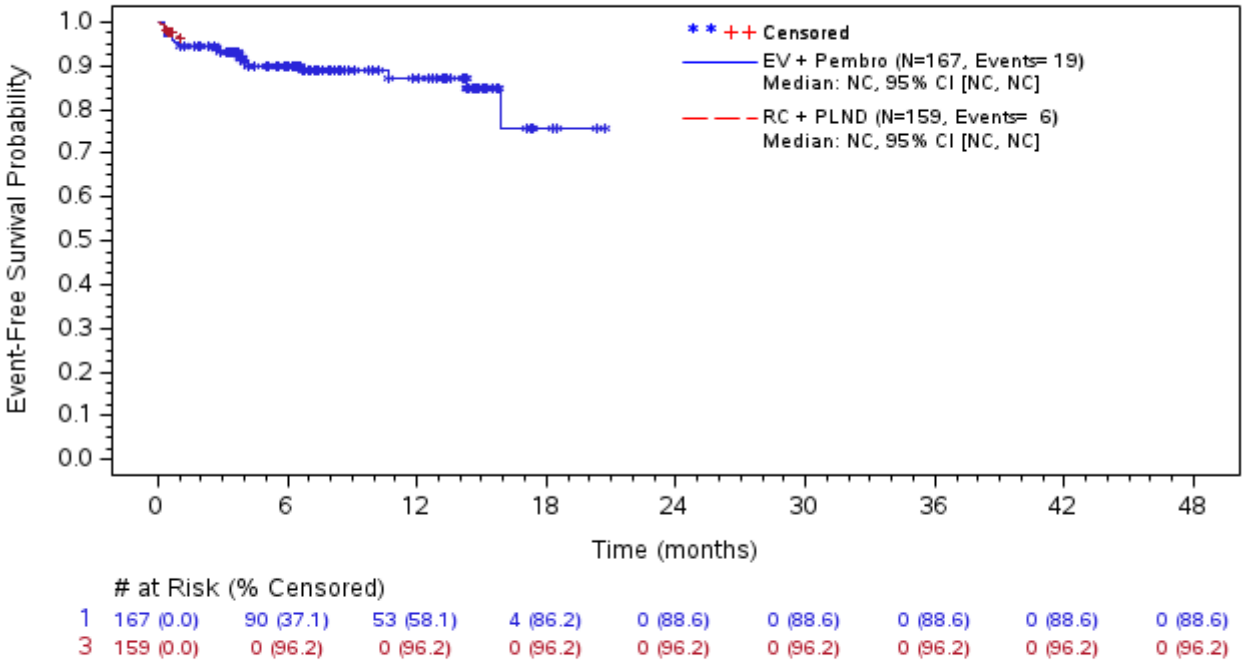
	# at Risk (% Censored)								
1	167 (0.0)	81 (29.3)	49 (47.3)	4 (73.7)	0 (76.0)	0 (76.0)	0 (76.0)	0 (76.0)	0 (76.0)
3	159 (0.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.34.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Blood Creatinine Increased (PT) - SAF2 Analysis Set



at Risk (% Censored)

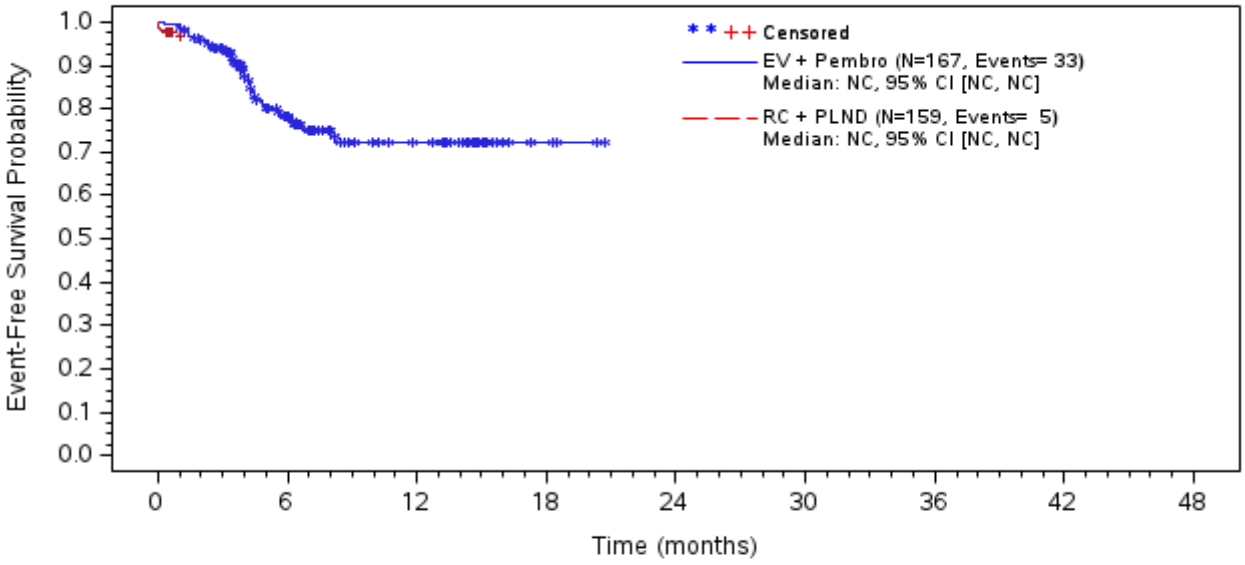
1	167 (0.0)	90 (37.1)	53 (58.1)	4 (86.2)	0 (88.6)	0 (88.6)	0 (88.6)	0 (88.6)	0 (88.6)
3	159 (0.0)	0 (96.2)	0 (96.2)	0 (96.2)	0 (96.2)	0 (96.2)	0 (96.2)	0 (96.2)	0 (96.2)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.35.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Weight Decreased (PT) - SAF2 Analysis Set



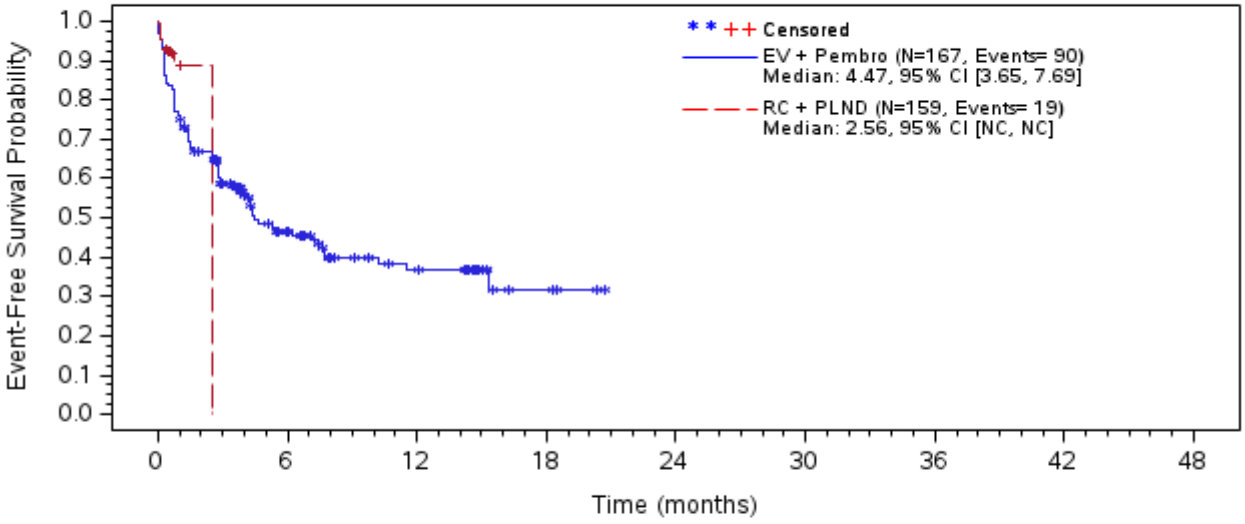
# at Risk (% Censored)									
1	167 (0.0)	78 (36.5)	42 (55.1)	4 (77.8)	0 (80.2)	0 (80.2)	0 (80.2)	0 (80.2)	0 (80.2)
3	159 (0.0)	0 (96.9)	0 (96.9)	0 (96.9)	0 (96.9)	0 (96.9)	0 (96.9)	0 (96.9)	0 (96.9)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.36.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Metabolism and Nutrition Disorders (SOC) - SAF2 Analysis Set



at Risk (% Censored)

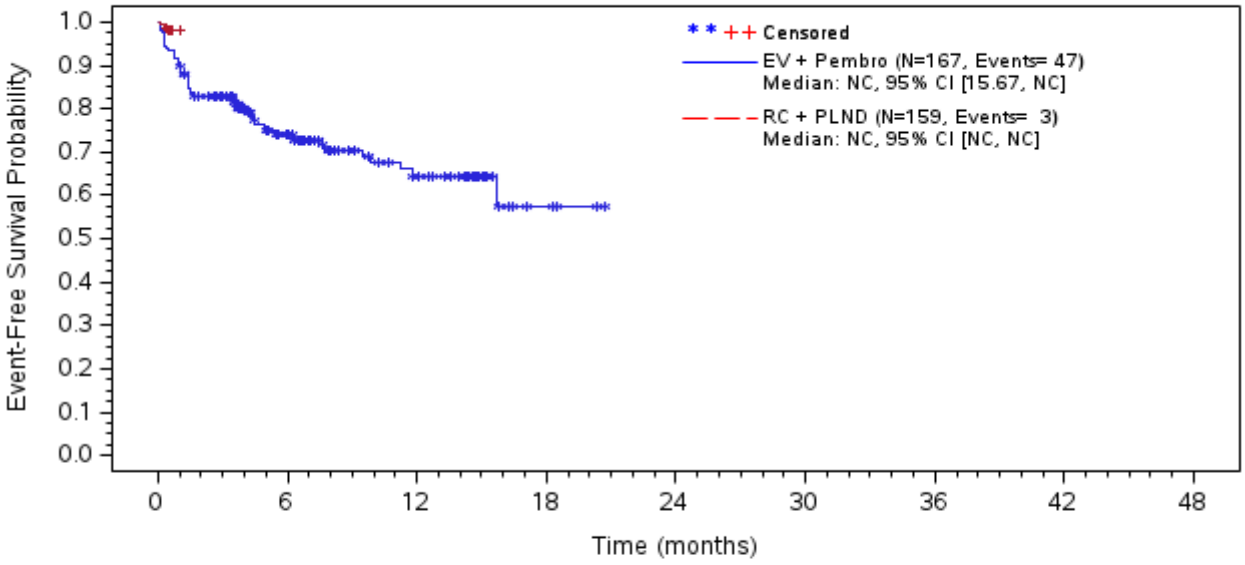
1	167 (0.0)	47 (23.4)	23 (32.9)	4 (43.7)	0 (46.1)	0 (46.1)	0 (46.1)	0 (46.1)	0 (46.1)
3	159 (0.0)	0 (88.1)	0 (88.1)	0 (88.1)	0 (88.1)	0 (88.1)	0 (88.1)	0 (88.1)	0 (88.1)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.37.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Decreased Appetite (PT) - SAF2 Analysis Set



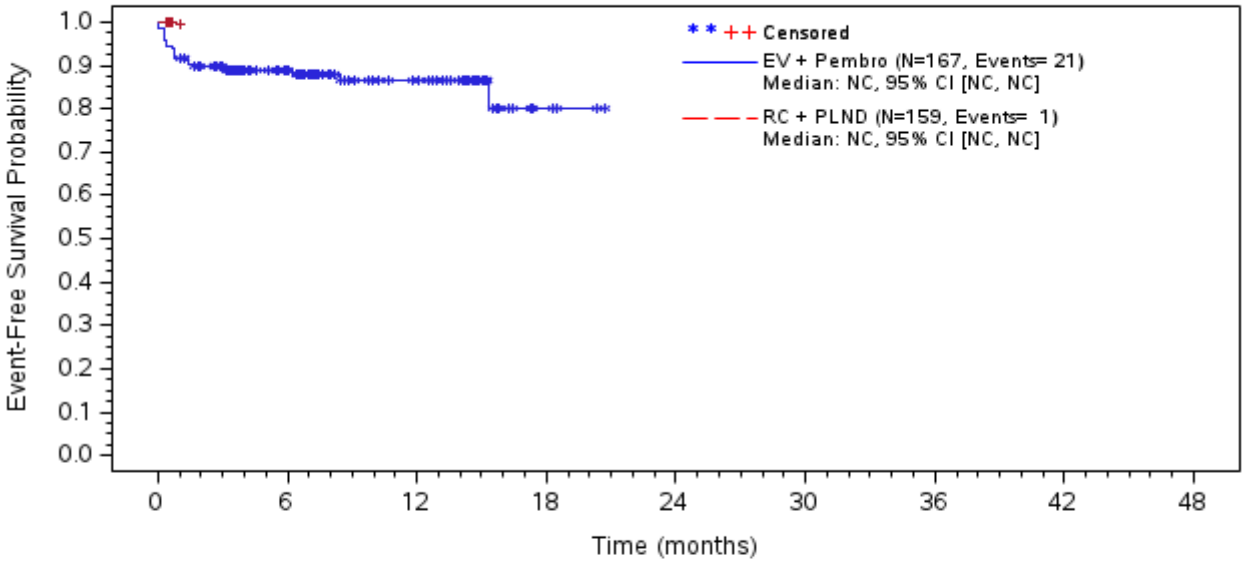
# at Risk (% Censored)									
1	167 (0.0)	77 (30.5)	40 (48.5)	4 (69.5)	0 (71.9)	0 (71.9)	0 (71.9)	0 (71.9)	0 (71.9)
3	159 (0.0)	0 (98.1)	0 (98.1)	0 (98.1)	0 (98.1)	0 (98.1)	0 (98.1)	0 (98.1)	0 (98.1)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.38.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Hyperglycaemia (PT) - SAF2 Analysis Set



at Risk (% Censored)

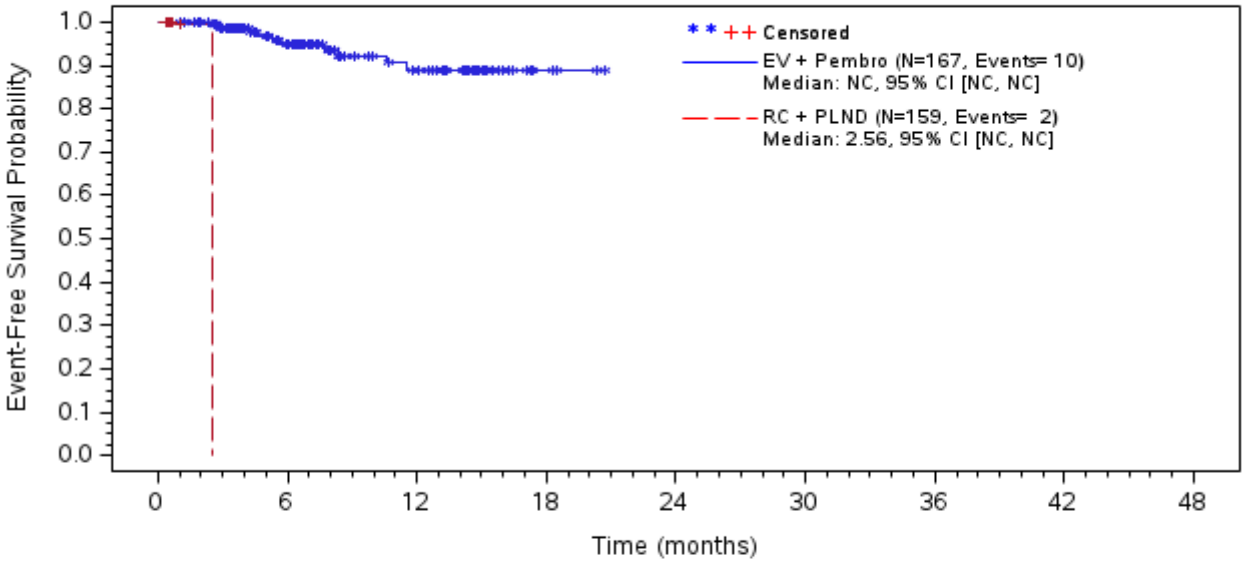
1	167 (0.0)	91 (34.7)	56 (54.5)	4 (85.0)	0 (87.4)	0 (87.4)	0 (87.4)	0 (87.4)	0 (87.4)
3	159 (0.0)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.39.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Hyperkalaemia (PT) - SAF2 Analysis Set



at Risk (% Censored)

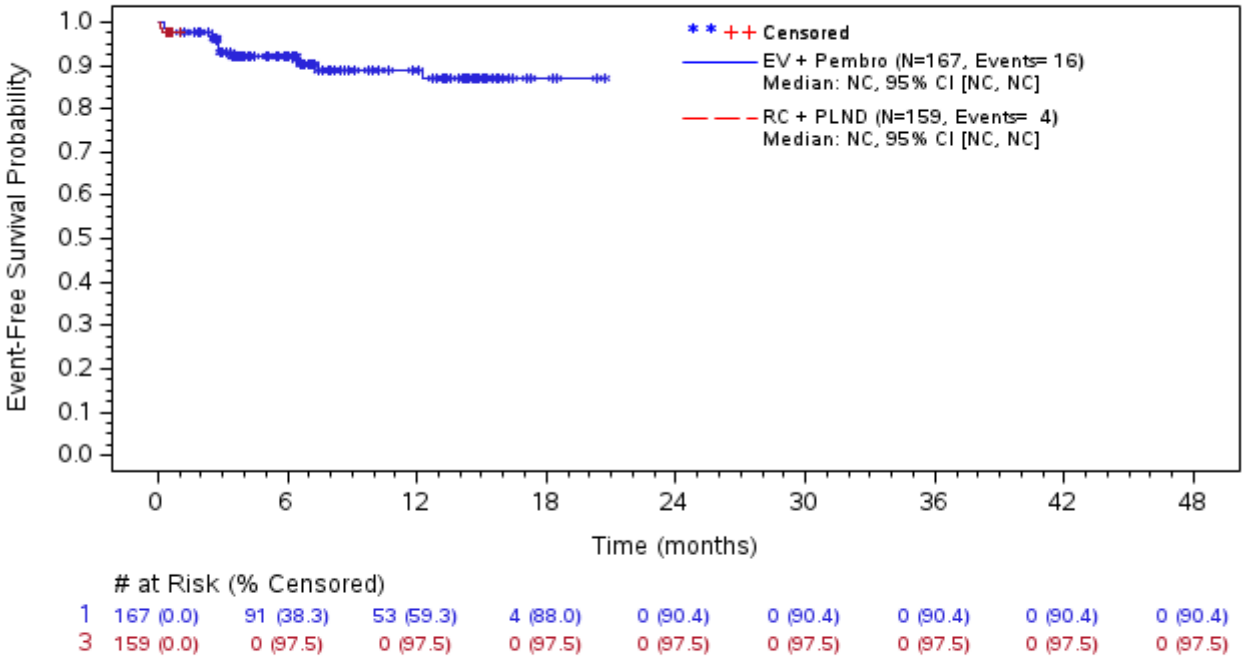
1	167 (0.0)	94 (40.1)	54 (61.7)	4 (91.6)	0 (94.0)	0 (94.0)	0 (94.0)	0 (94.0)	0 (94.0)
3	159 (0.0)	0 (98.7)	0 (98.7)	0 (98.7)	0 (98.7)	0 (98.7)	0 (98.7)	0 (98.7)	0 (98.7)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.40.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Hypokalaemia (PT) - SAF2 Analysis Set



at Risk (% Censored)

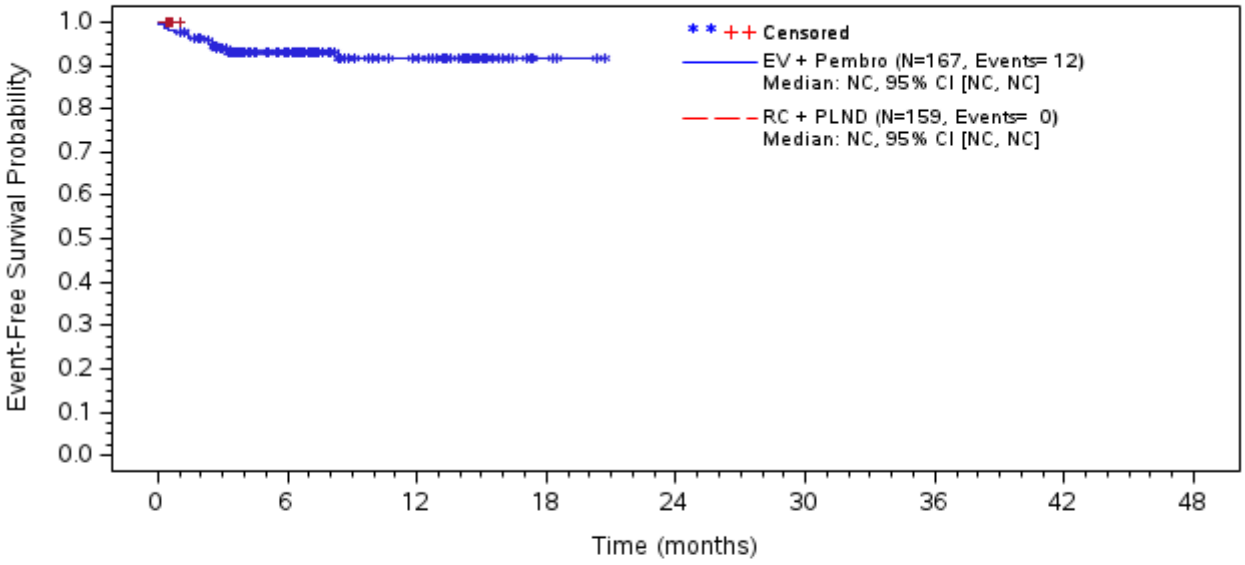
1	167 (0.0)	91 (38.3)	53 (59.3)	4 (88.0)	0 (90.4)	0 (90.4)	0 (90.4)	0 (90.4)	0 (90.4)
3	159 (0.0)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.41.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Hyponatraemia (PT) - SAF2 Analysis Set



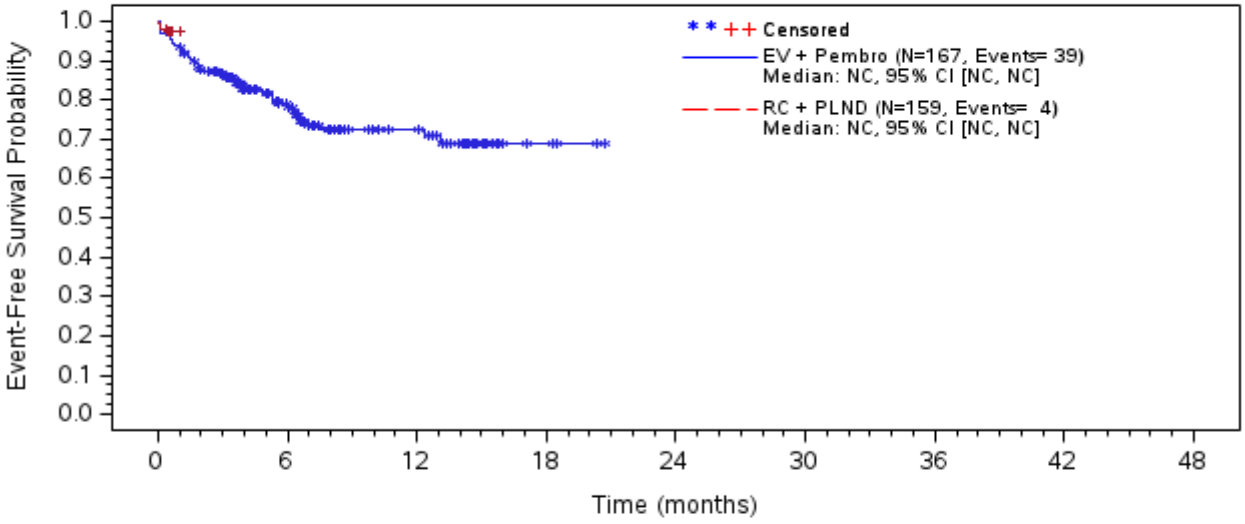
# at Risk (% Censored)									
1	167 (0.0)	93 (37.7)	56 (59.3)	4 (90.4)	0 (92.8)	0 (92.8)	0 (92.8)	0 (92.8)	0 (92.8)
3	159 (0.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.42.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Musculoskeletal and Connective Tissue Disorders (SOC) - SAF2 Analysis Set



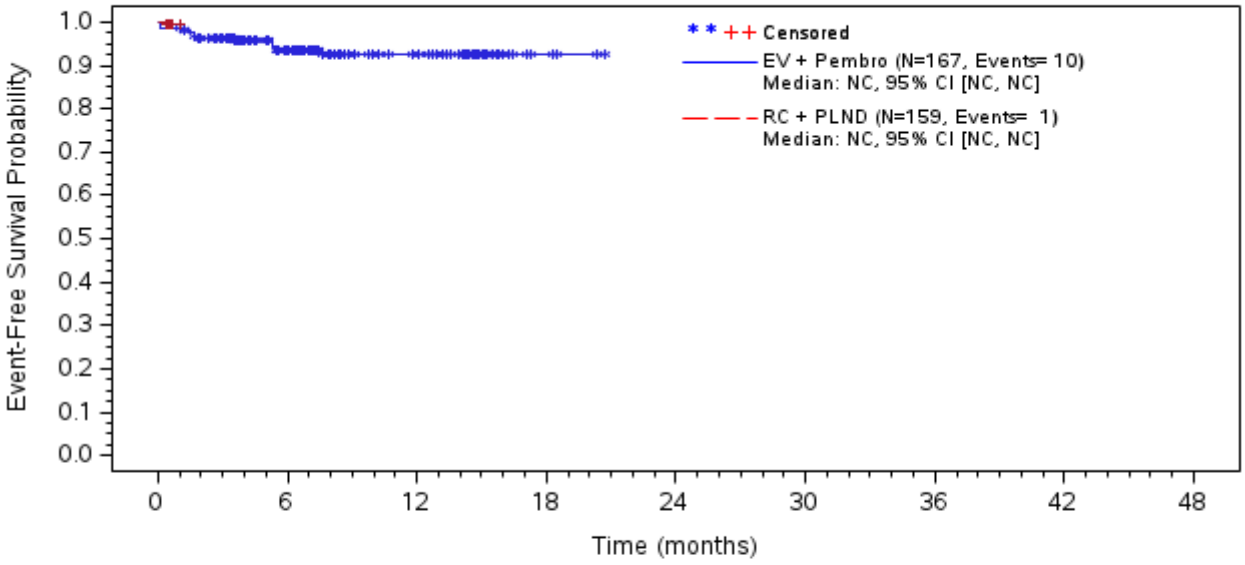
	# at Risk (% Censored)								
1	167 (0.0)	79 (34.1)	45 (50.9)	4 (74.3)	0 (76.6)	0 (76.6)	0 (76.6)	0 (76.6)	0 (76.6)
3	159 (0.0)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.43.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Arthralgia (PT) - SAF2 Analysis Set



at Risk (% Censored)

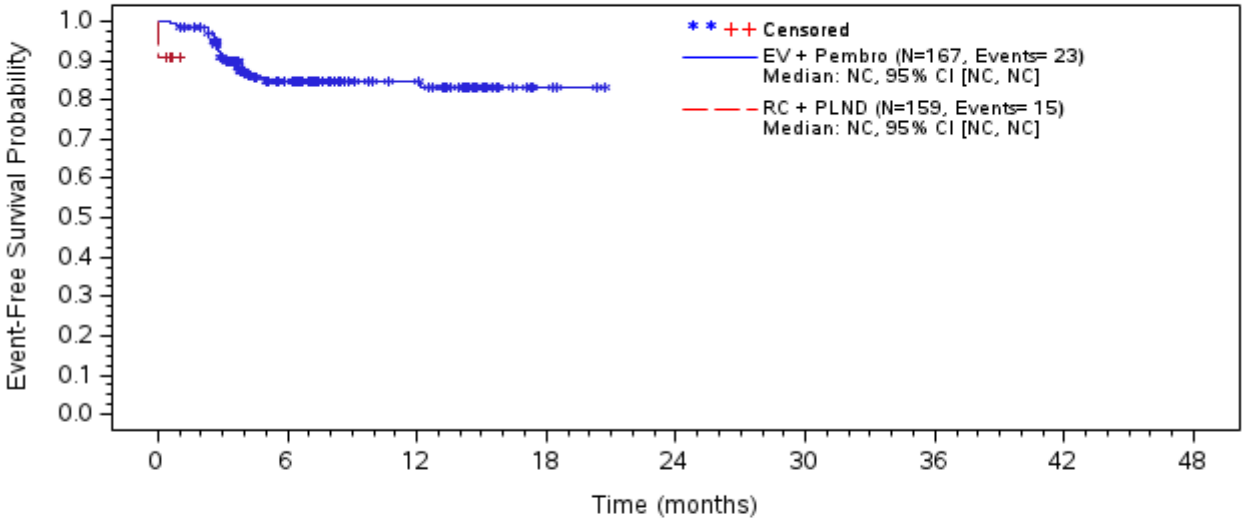
1	167 (0.0)	92 (39.5)	55 (61.1)	4 (91.6)	0 (94.0)	0 (94.0)	0 (94.0)	0 (94.0)	0 (94.0)
3	159 (0.0)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.44.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Neoplasms Benign, Malignant and Unspecified (Incl Cysts and Polyps) (SOC) - SAF2 Analysis Set



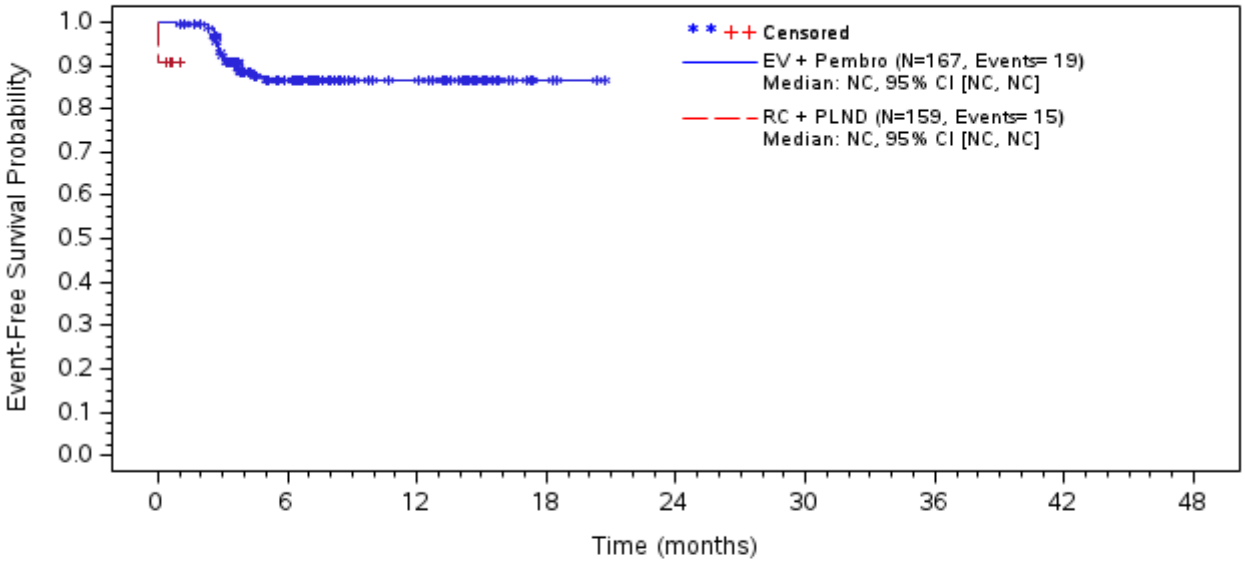
# at Risk (% Censored)									
1	167 (0.0)	86 (35.3)	52 (55.7)	4 (83.8)	0 (86.2)	0 (86.2)	0 (86.2)	0 (86.2)	0 (86.2)
3	159 (0.0)	0 (90.6)	0 (90.6)	0 (90.6)	0 (90.6)	0 (90.6)	0 (90.6)	0 (90.6)	0 (90.6)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.45.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Prostate Cancer (PT) - SAF2 Analysis Set



at Risk (% Censored)

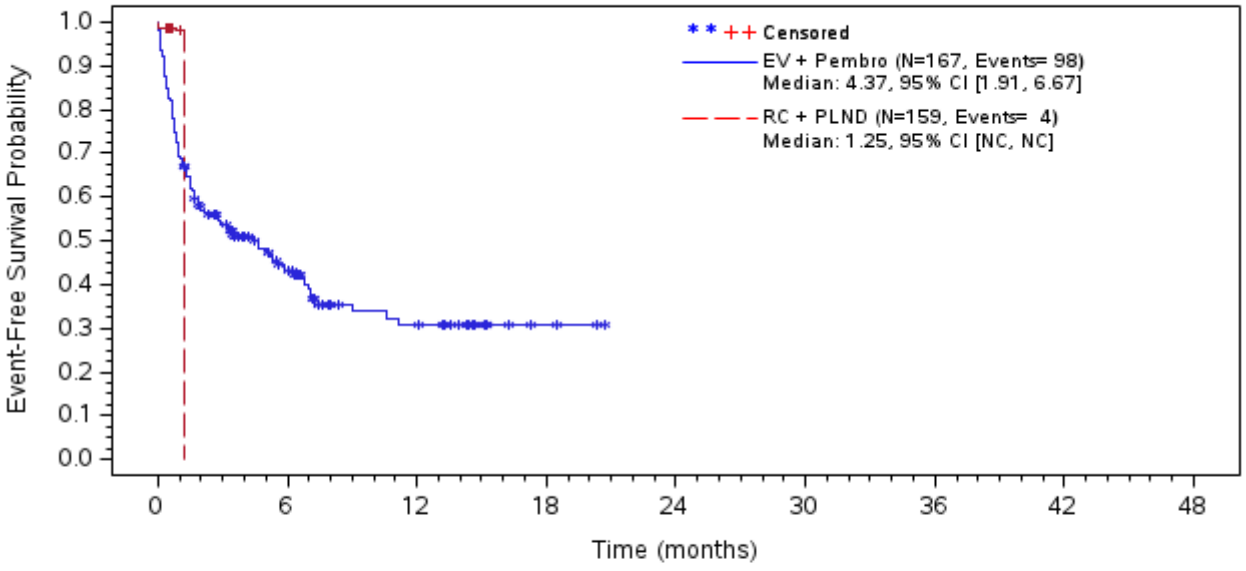
1	167 (0.0)	86 (37.1)	52 (57.5)	4 (86.2)	0 (88.6)	0 (88.6)	0 (88.6)	0 (88.6)	0 (88.6)
3	159 (0.0)	0 (90.6)	0 (90.6)	0 (90.6)	0 (90.6)	0 (90.6)	0 (90.6)	0 (90.6)	0 (90.6)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.46.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Nervous System Disorders (SOC) - SAF2 Analysis Set



at Risk (% Censored)

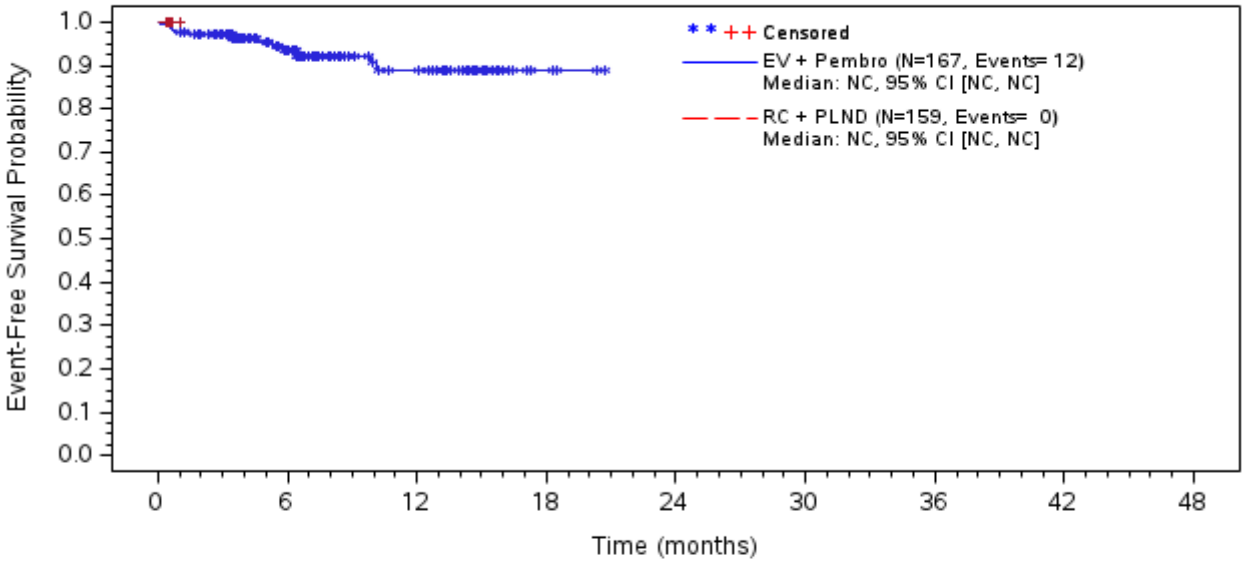
1	167 (0.0)	44 (21.0)	20 (29.3)	3 (39.5)	0 (41.3)	0 (41.3)	0 (41.3)	0 (41.3)	0 (41.3)
3	159 (0.0)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.47.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Dizziness (PT) - SAF2 Analysis Set



at Risk (% Censored)

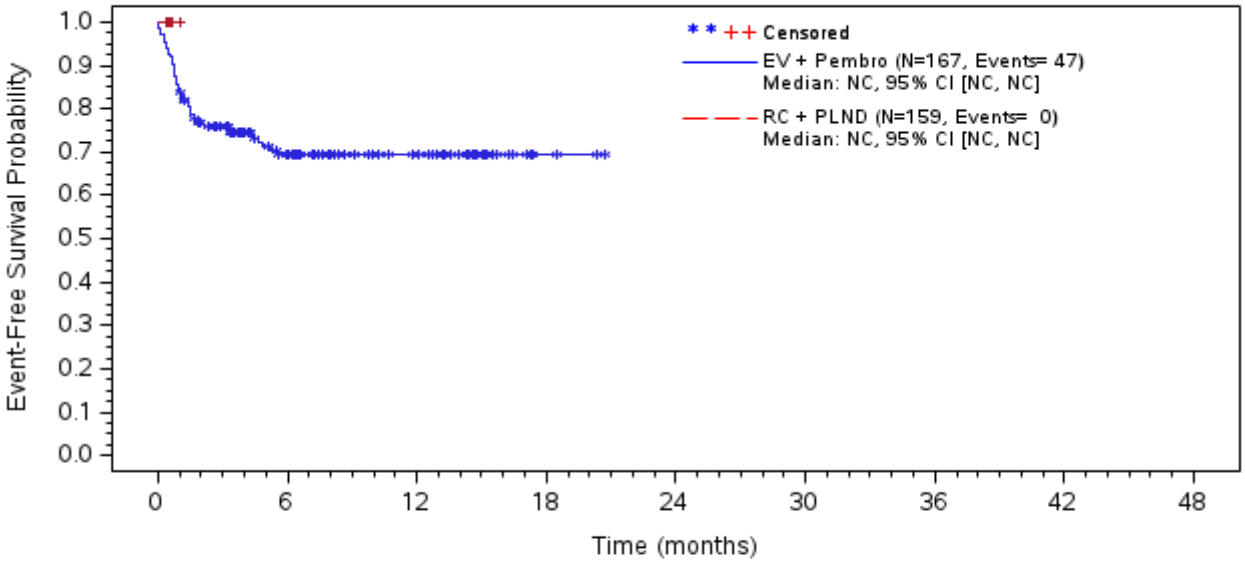
1	167 (0.0)	90 (40.7)	53 (61.1)	4 (90.4)	0 (92.8)	0 (92.8)	0 (92.8)	0 (92.8)	0 (92.8)
3	159 (0.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.48.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Dysgeusia (PT) - SAF2 Analysis Set



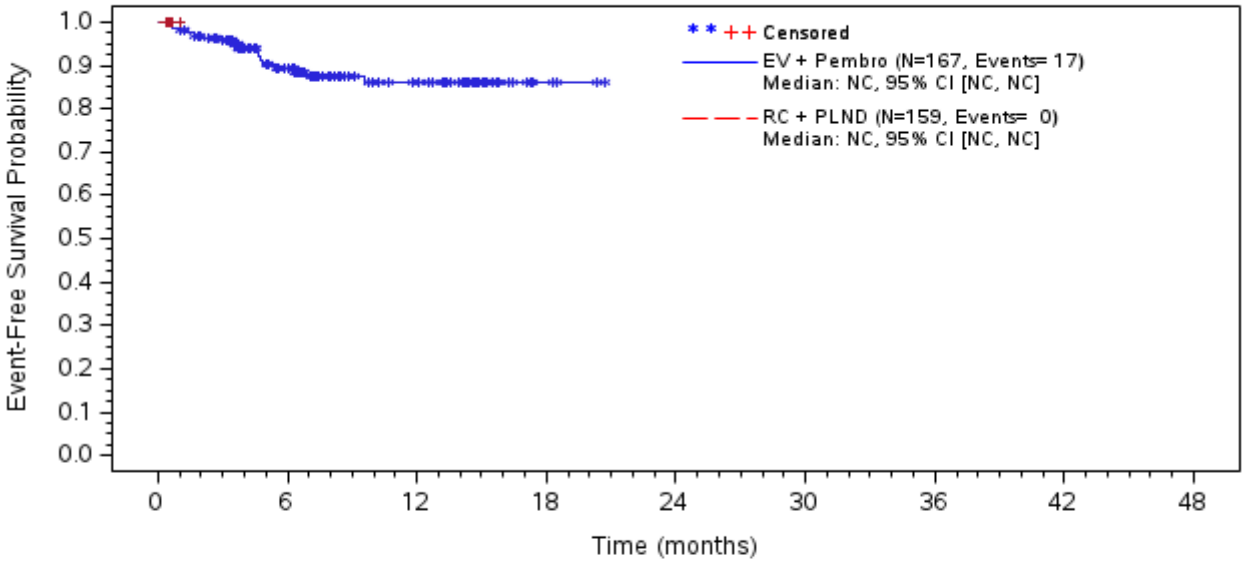
# at Risk (% Censored)									
1	167 (0.0)	68 (31.1)	39 (48.5)	3 (70.1)	0 (71.9)	0 (71.9)	0 (71.9)	0 (71.9)	0 (71.9)
3	159 (0.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.49.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Neuropathy Peripheral (PT) - SAF2 Analysis Set



at Risk (% Censored)

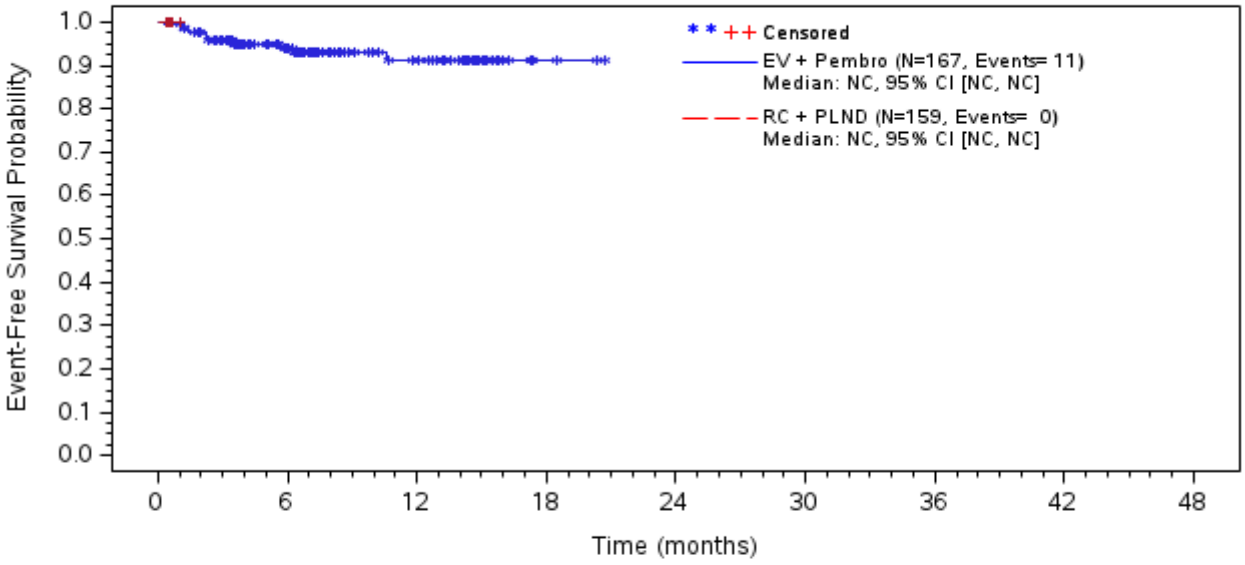
1	167 (0.0)	91 (37.1)	52 (58.7)	4 (87.4)	0 (89.8)	0 (89.8)	0 (89.8)	0 (89.8)	0 (89.8)
3	159 (0.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.50.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Paraesthesia (PT) - SAF2 Analysis Set



at Risk (% Censored)

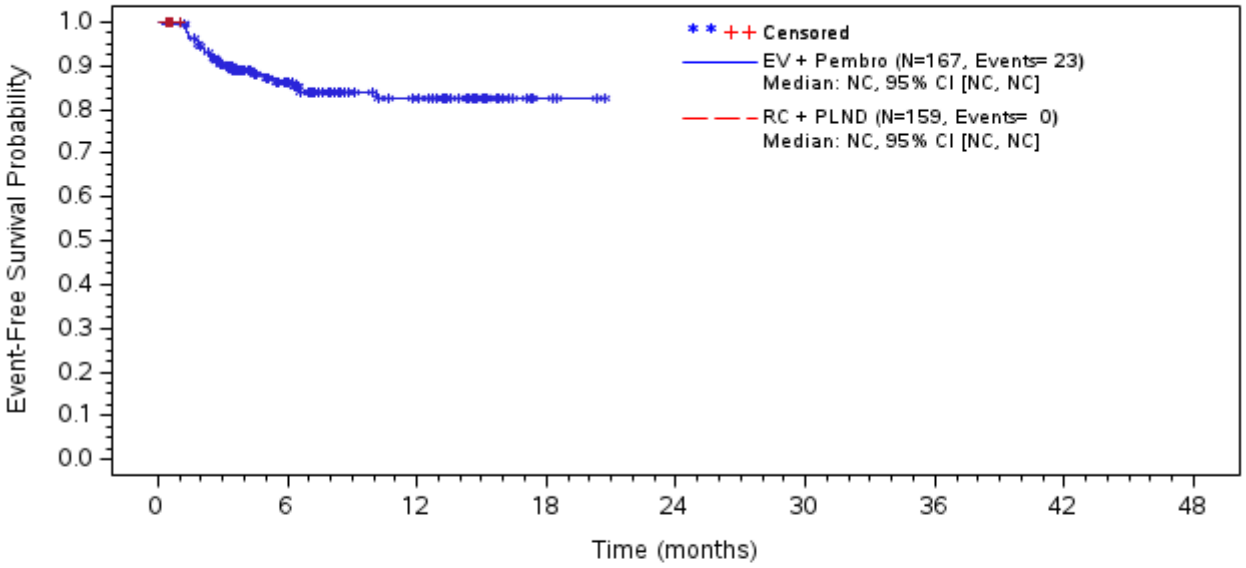
1	167 (0.0)	93 (38.9)	53 (61.7)	3 (91.6)	0 (93.4)	0 (93.4)	0 (93.4)	0 (93.4)	0 (93.4)
3	159 (0.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.51.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Peripheral Sensory Neuropathy (PT) - SAF2 Analysis Set



at Risk (% Censored)

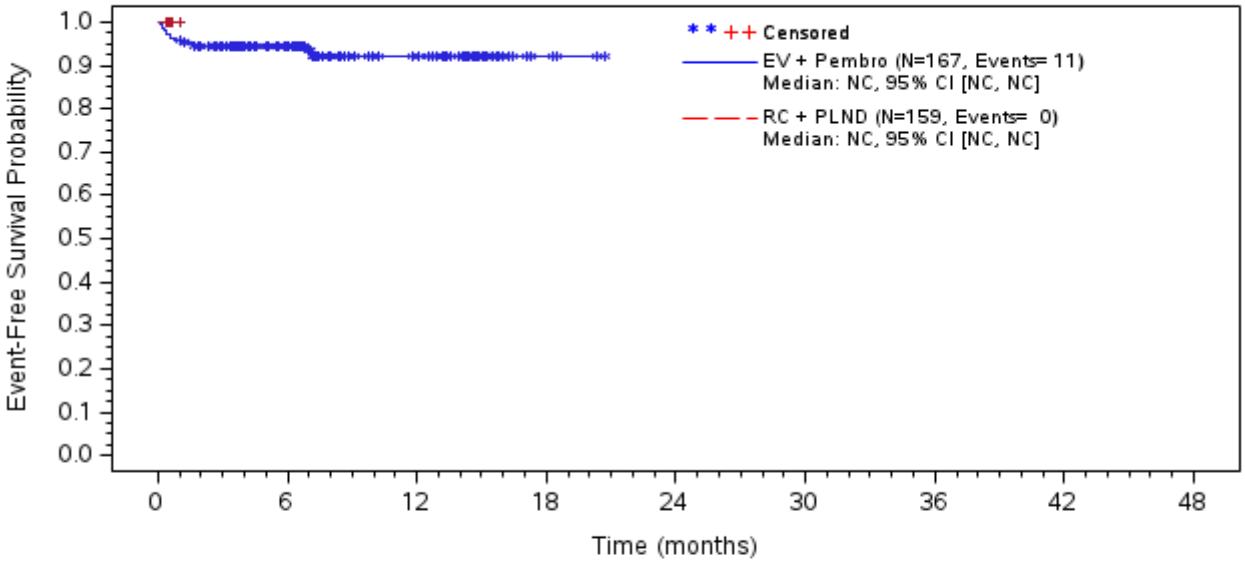
1	167 (0.0)	83 (38.3)	50 (56.3)	4 (83.8)	0 (86.2)	0 (86.2)	0 (86.2)	0 (86.2)	0 (86.2)
3	159 (0.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.52.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Taste Disorder (PT) - SAF2 Analysis Set



at Risk (% Censored)

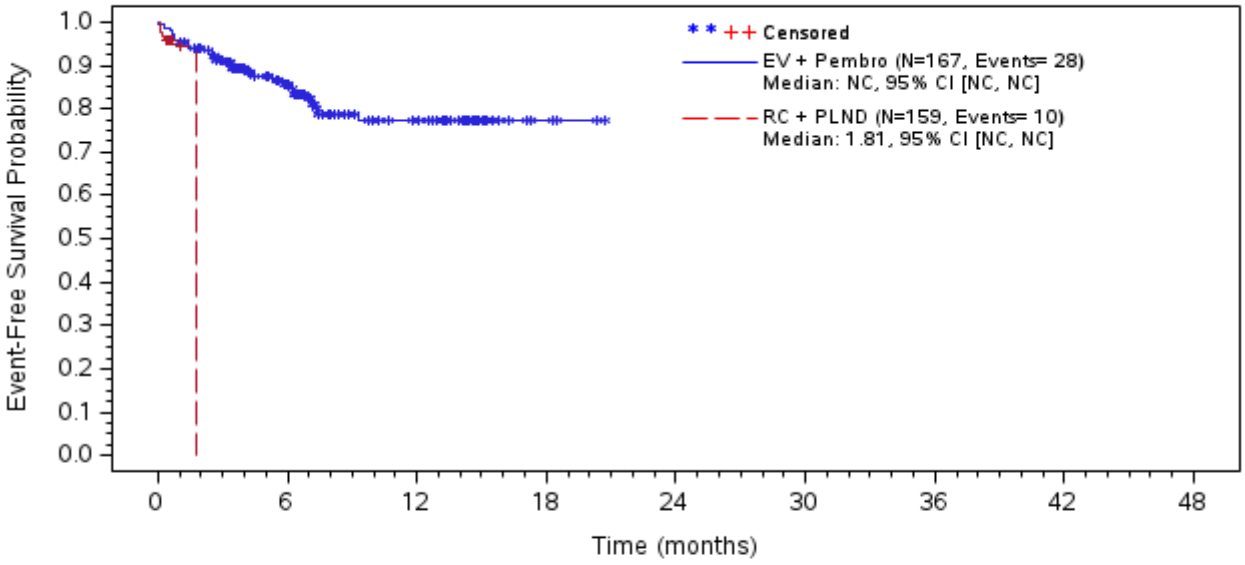
1	167 (0.0)	94 (38.3)	59 (58.1)	4 (91.0)	0 (93.4)	0 (93.4)	0 (93.4)	0 (93.4)	0 (93.4)
3	159 (0.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.53.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Psychiatric Disorders (SOC) - SAF2 Analysis Set



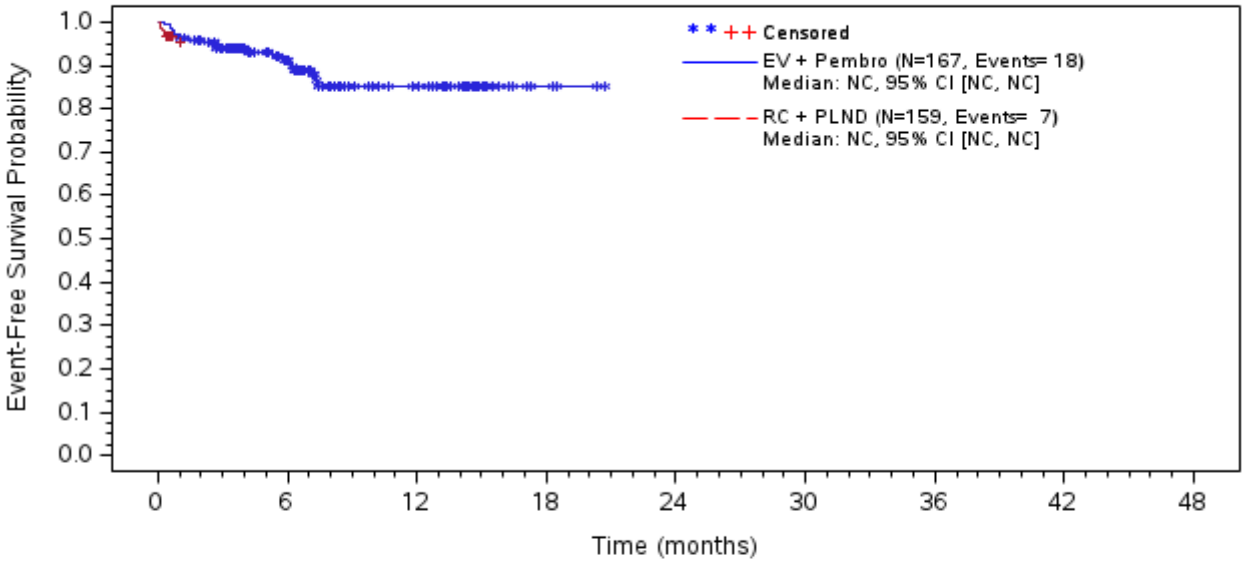
	# at Risk (% Censored)								
1	167 (0.0)	85 (36.5)	46 (55.7)	4 (80.8)	0 (83.2)	0 (83.2)	0 (83.2)	0 (83.2)	0 (83.2)
3	159 (0.0)	0 (93.7)	0 (93.7)	0 (93.7)	0 (93.7)	0 (93.7)	0 (93.7)	0 (93.7)	0 (93.7)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.54.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Insomnia (PT) - SAF2 Analysis Set



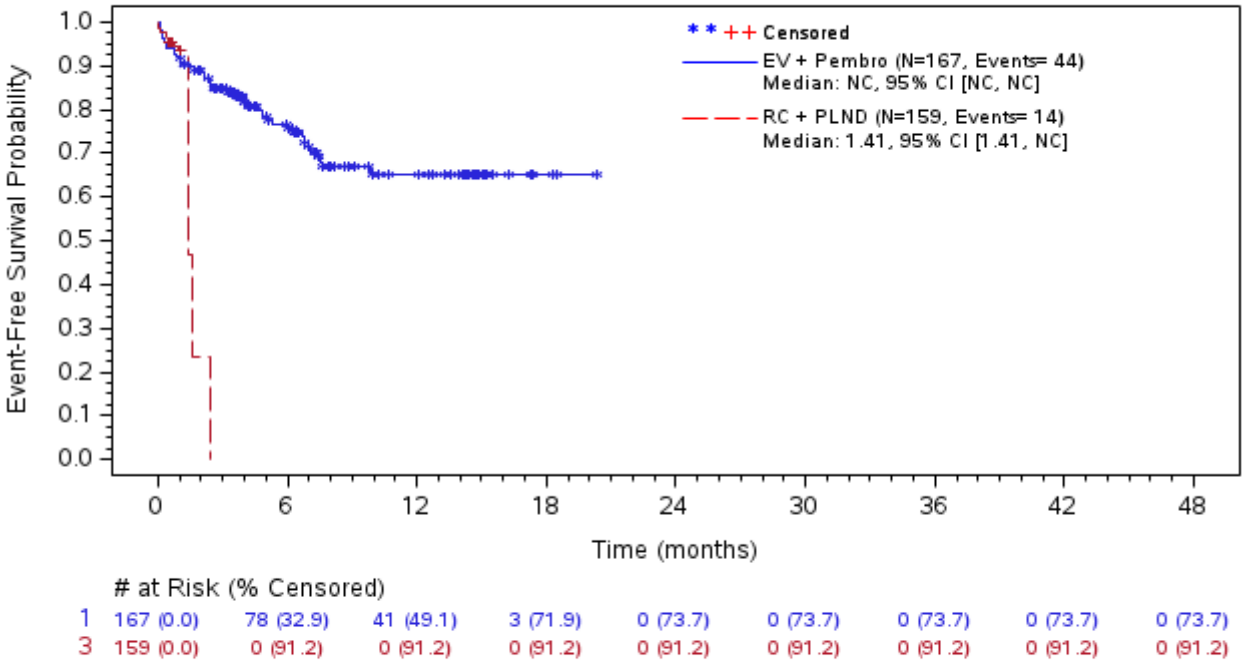
	# at Risk (% Censored)								
1	167 (0.0)	90 (38.3)	50 (59.3)	4 (86.8)	0 (89.2)	0 (89.2)	0 (89.2)	0 (89.2)	0 (89.2)
3	159 (0.0)	0 (95.6)	0 (95.6)	0 (95.6)	0 (95.6)	0 (95.6)	0 (95.6)	0 (95.6)	0 (95.6)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.55.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Renal and Urinary Disorders (SOC) - SAF2 Analysis Set



at Risk (% Censored)

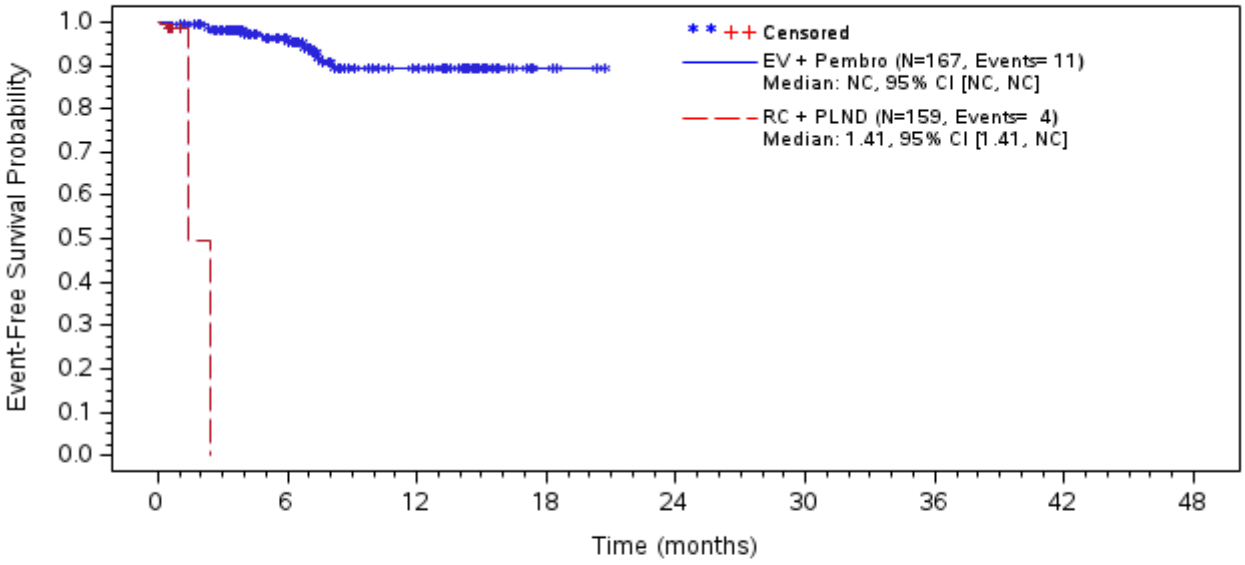
1	167 (0.0)	78 (32.9)	41 (49.1)	3 (71.9)	0 (73.7)	0 (73.7)	0 (73.7)	0 (73.7)	0 (73.7)
3	159 (0.0)	0 (91.2)	0 (91.2)	0 (91.2)	0 (91.2)	0 (91.2)	0 (91.2)	0 (91.2)	0 (91.2)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.56.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Acute Kidney Injury (PT) - SAF2 Analysis Set



at Risk (% Censored)

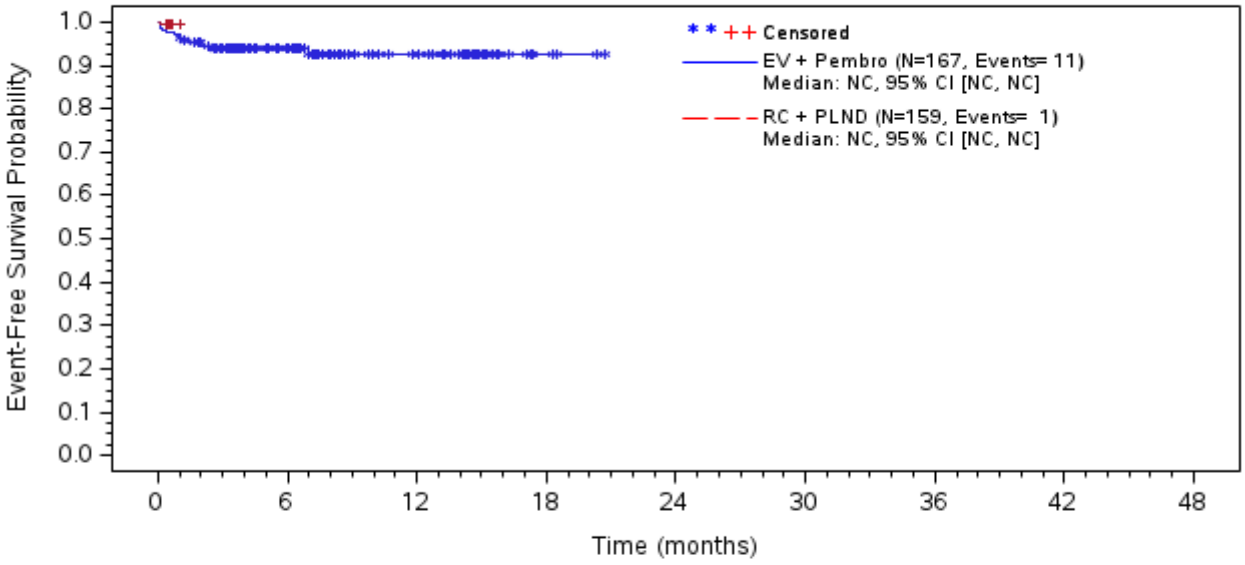
1	167 (0.0)	95 (40.1)	54 (61.1)	4 (91.0)	0 (93.4)	0 (93.4)	0 (93.4)	0 (93.4)	0 (93.4)
3	159 (0.0)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.57.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Haematuria (PT) - SAF2 Analysis Set



at Risk (% Censored)

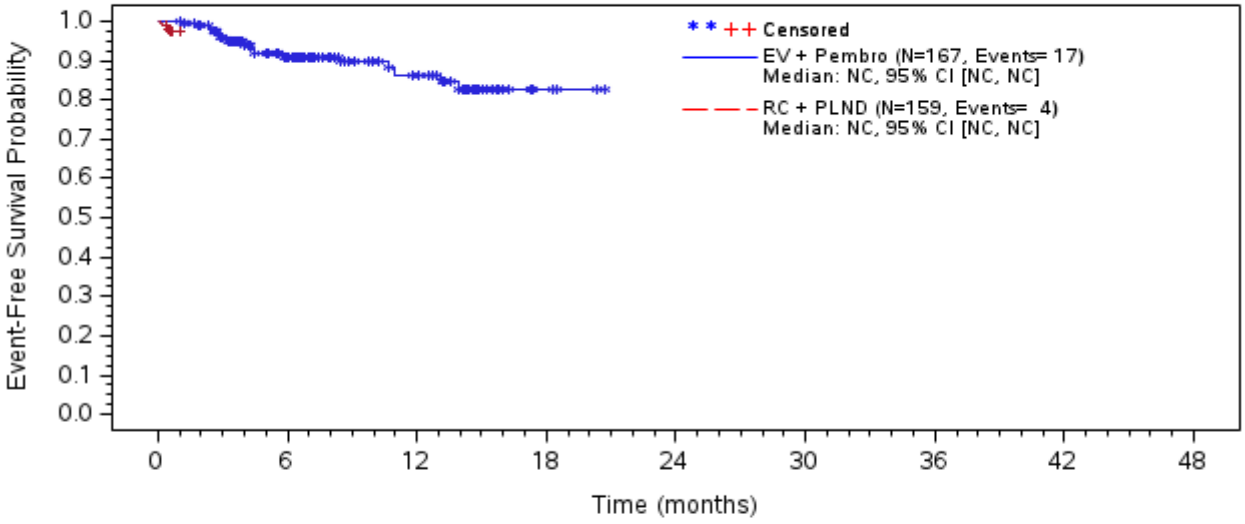
1	167 (0.0)	92 (38.9)	54 (61.1)	4 (91.0)	0 (93.4)	0 (93.4)	0 (93.4)	0 (93.4)	0 (93.4)
3	159 (0.0)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.58.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Reproductive System and Breast Disorders (SOC) - SAF2 Analysis Set



at Risk (% Censored)

1	167 (0.0)	91 (38.3)	52 (59.9)	4 (87.4)	0 (89.8)	0 (89.8)	0 (89.8)	0 (89.8)	0 (89.8)
3	159 (0.0)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)

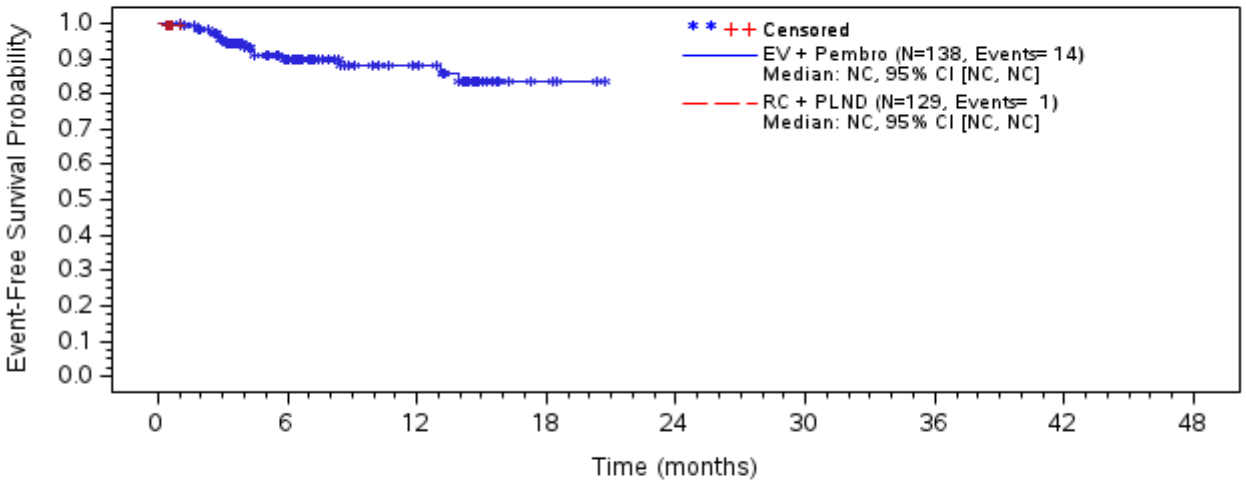
Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.58.1.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases by Cisplatin Eligibility - Reproductive System and Breast Disorders (SOC) - SAF2 Analysis Set

Cisplatin Eligibility: Ineligible



at Risk (% Censored)

1	138 (0.0)	72 (39.9)	41 (61.6)	4 (87.0)	0 (89.9)	0 (89.9)	0 (89.9)	0 (89.9)	0 (89.9)
3	129 (0.0)	0 (99.2)	0 (99.2)	0 (99.2)	0 (99.2)	0 (99.2)	0 (99.2)	0 (99.2)	0 (99.2)

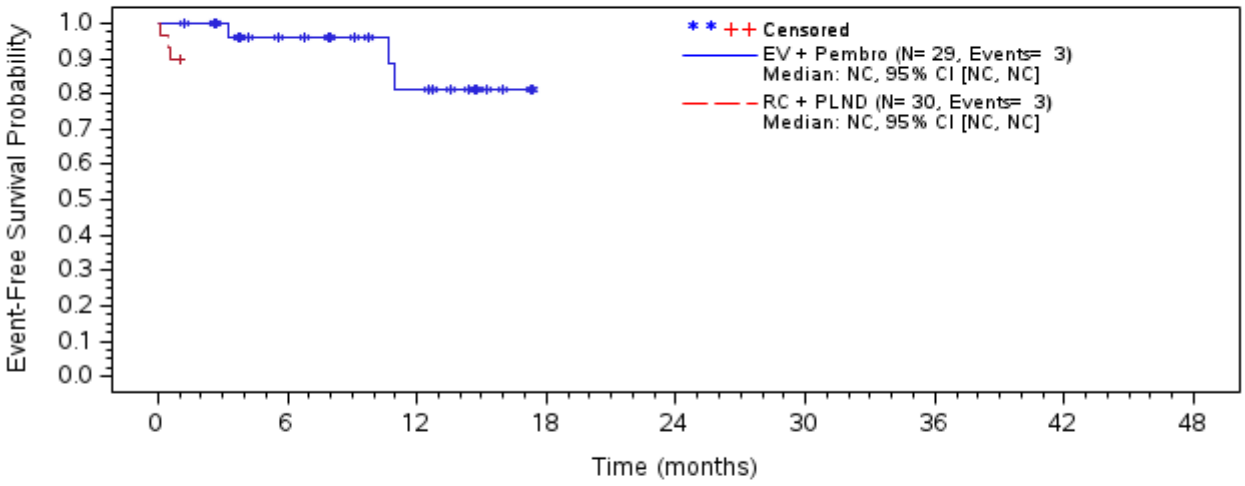
Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.58.1.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases by Cisplatin Eligibility - Reproductive System and Breast Disorders (SOC) - SAF2 Analysis Set

Cisplatin Eligibility: Eligible but Declined



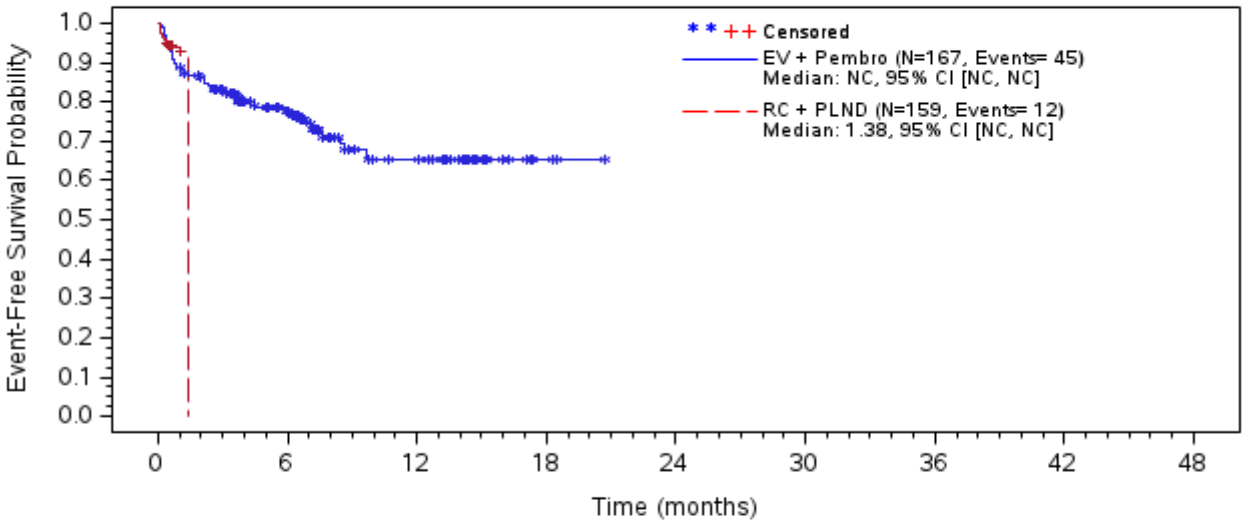
# at Risk (% Censored)									
1	29 (0.0)	19 (31.0)	11 (51.7)	0 (89.7)	0 (89.7)	0 (89.7)	0 (89.7)	0 (89.7)	0 (89.7)
3	30 (0.0)	0 (90.0)	0 (90.0)	0 (90.0)	0 (90.0)	0 (90.0)	0 (90.0)	0 (90.0)	0 (90.0)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.59.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Respiratory, Thoracic and Mediastinal Disorders (SOC) - SAF2 Analysis Set



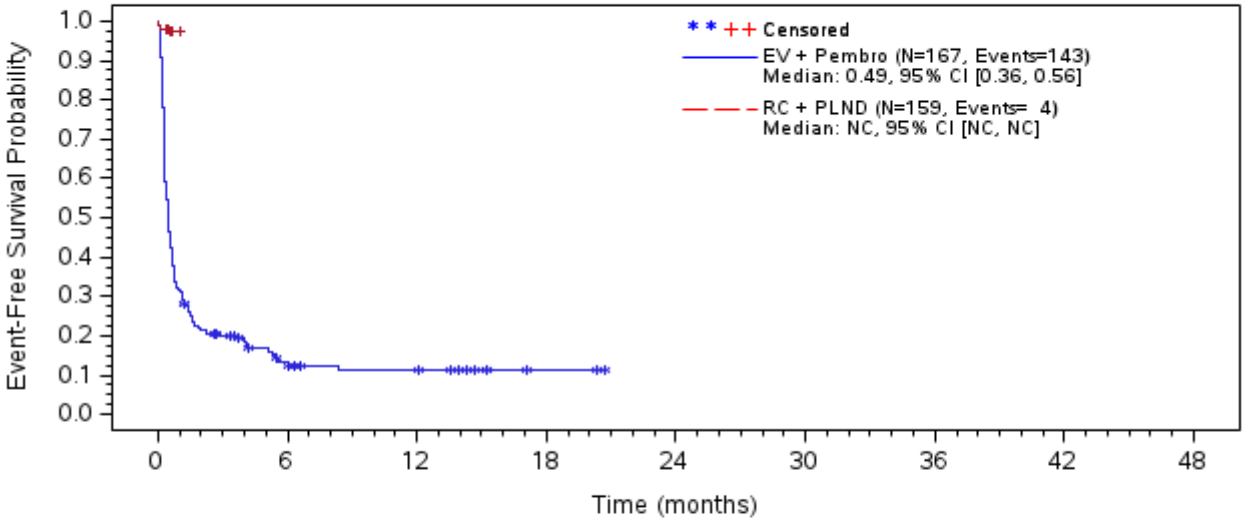
	# at Risk (% Censored)								
1	167 (0.0)	80 (31.1)	41 (48.5)	3 (71.3)	0 (73.1)	0 (73.1)	0 (73.1)	0 (73.1)	0 (73.1)
3	159 (0.0)	0 (92.5)	0 (92.5)	0 (92.5)	0 (92.5)	0 (92.5)	0 (92.5)	0 (92.5)	0 (92.5)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.60.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Skin and Subcutaneous Tissue Disorders (SOC) - SAF2 Analysis Set



	# at Risk (% Censored)								
1	167 (0.0)	15 (6.6)	10 (8.4)	2 (13.2)	0 (14.4)	0 (14.4)	0 (14.4)	0 (14.4)	0 (14.4)
3	159 (0.0)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)

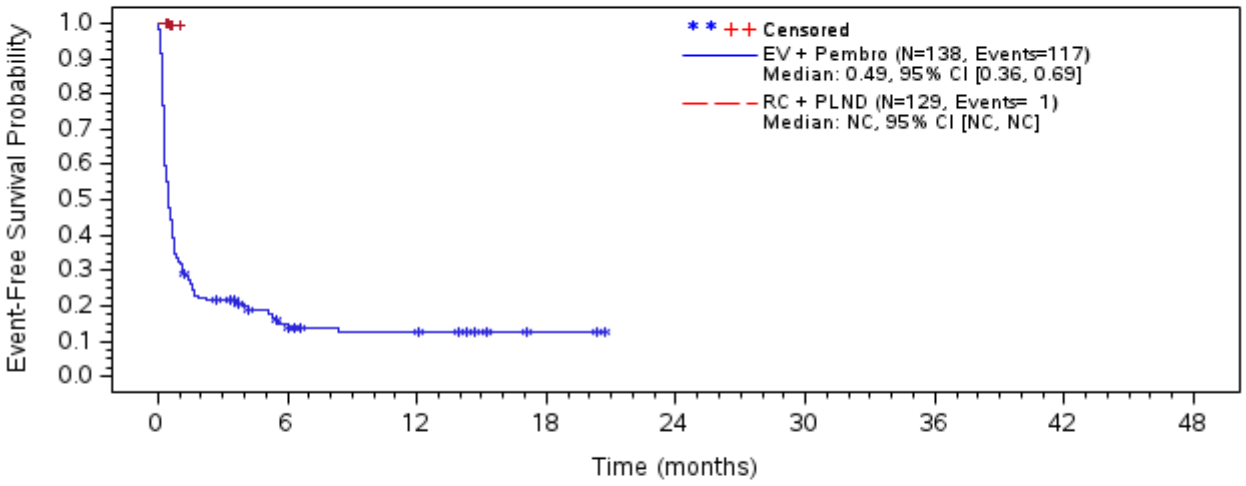
Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.60.1.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases by Cisplatin Eligibility - Skin and Subcutaneous Tissue Disorders (SOC) - SAF2 Analysis Set

Cisplatin Eligibility: Ineligible



	# at Risk (% Censored)								
1	138 (0.0)	14 (6.5)	9 (8.7)	2 (13.8)	0 (15.2)	0 (15.2)	0 (15.2)	0 (15.2)	0 (15.2)
3	129 (0.0)	0 (99.2)	0 (99.2)	0 (99.2)	0 (99.2)	0 (99.2)	0 (99.2)	0 (99.2)	0 (99.2)

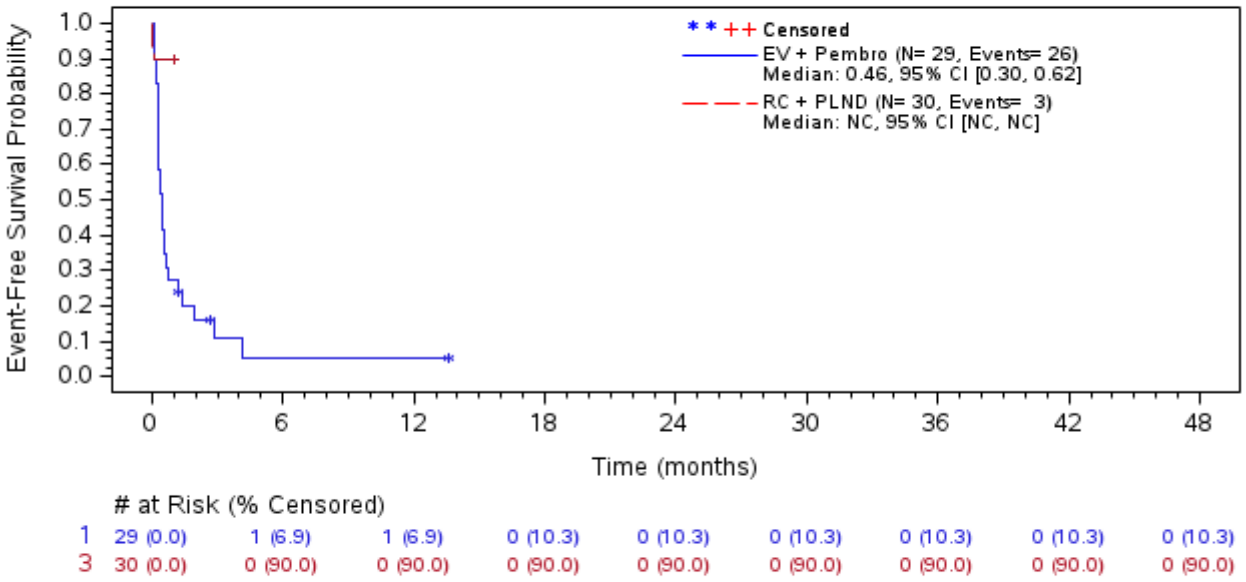
Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.60.1.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases by Cisplatin Eligibility - Skin and Subcutaneous Tissue Disorders (SOC) - SAF2 Analysis Set

Cisplatin Eligibility: Eligible but Declined



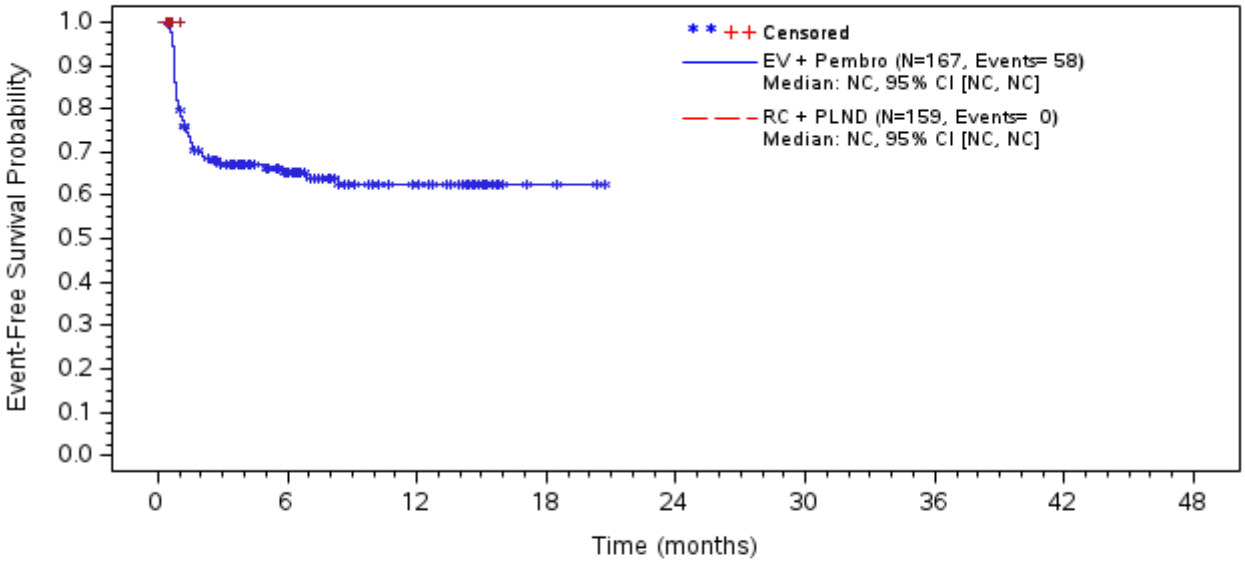
	# at Risk (% Censored)								
1	29 (0.0)	1 (6.9)	1 (6.9)	0 (10.3)	0 (10.3)	0 (10.3)	0 (10.3)	0 (10.3)	0 (10.3)
3	30 (0.0)	0 (90.0)	0 (90.0)	0 (90.0)	0 (90.0)	0 (90.0)	0 (90.0)	0 (90.0)	0 (90.0)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.61.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Alopecia (PT) - SAF2 Analysis Set



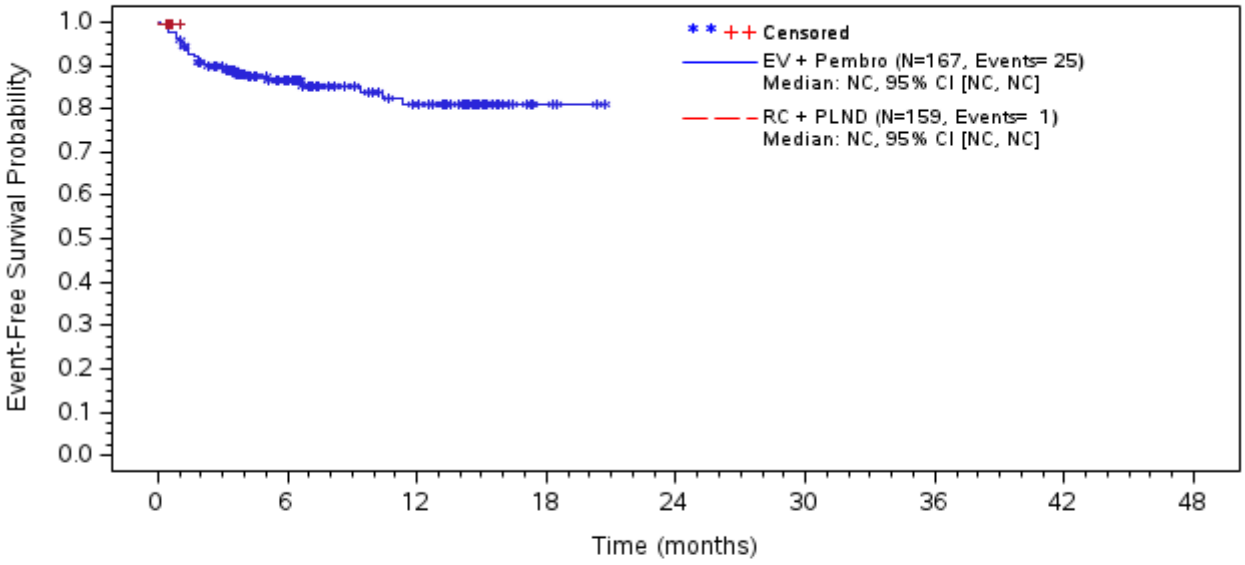
# at Risk (% Censored)									
1	167 (0.0)	64 (28.1)	35 (44.3)	3 (63.5)	0 (65.3)	0 (65.3)	0 (65.3)	0 (65.3)	0 (65.3)
3	159 (0.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.62.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Dry Skin (PT) - SAF2 Analysis Set



at Risk (% Censored)

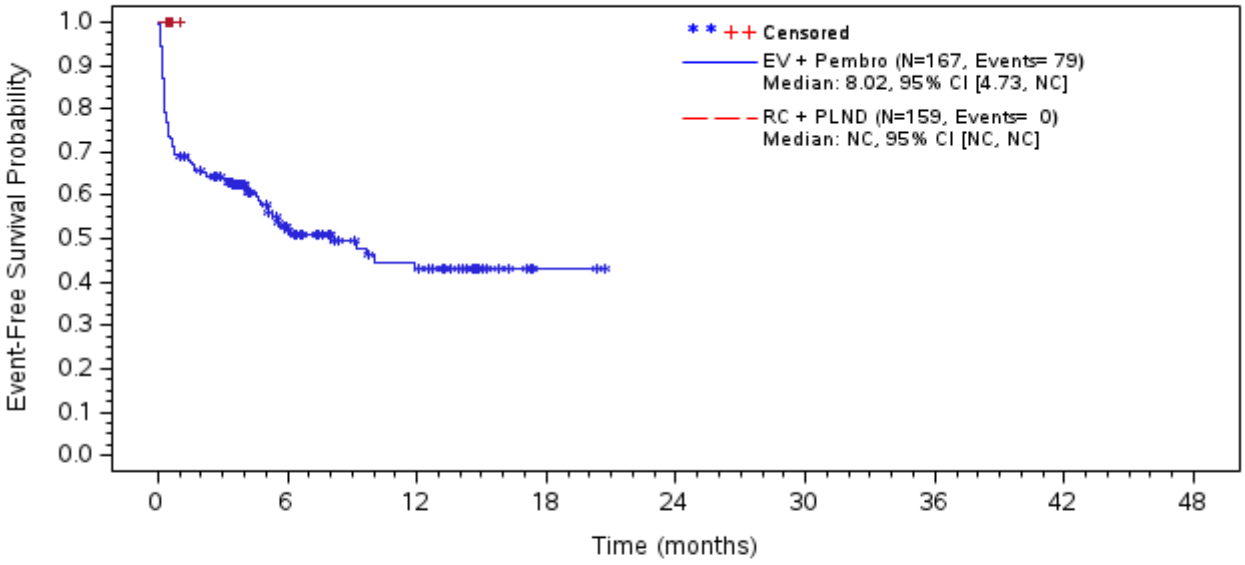
1	167 (0.0)	85 (36.5)	52 (53.9)	4 (82.6)	0 (85.0)	0 (85.0)	0 (85.0)	0 (85.0)	0 (85.0)
3	159 (0.0)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.63.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Pruritus (PT) - SAF2 Analysis Set



at Risk (% Censored)

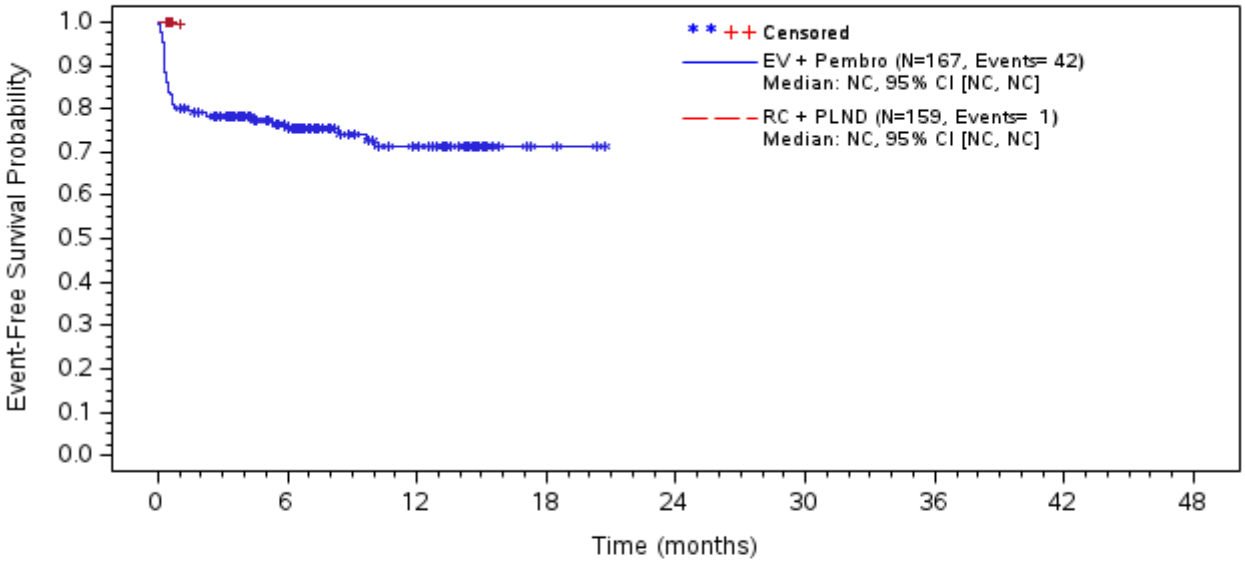
1	167 (0.0)	51 (26.3)	26 (37.1)	2 (51.5)	0 (52.7)	0 (52.7)	0 (52.7)	0 (52.7)	0 (52.7)
3	159 (0.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.64.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Rash (PT) - SAF2 Analysis Set



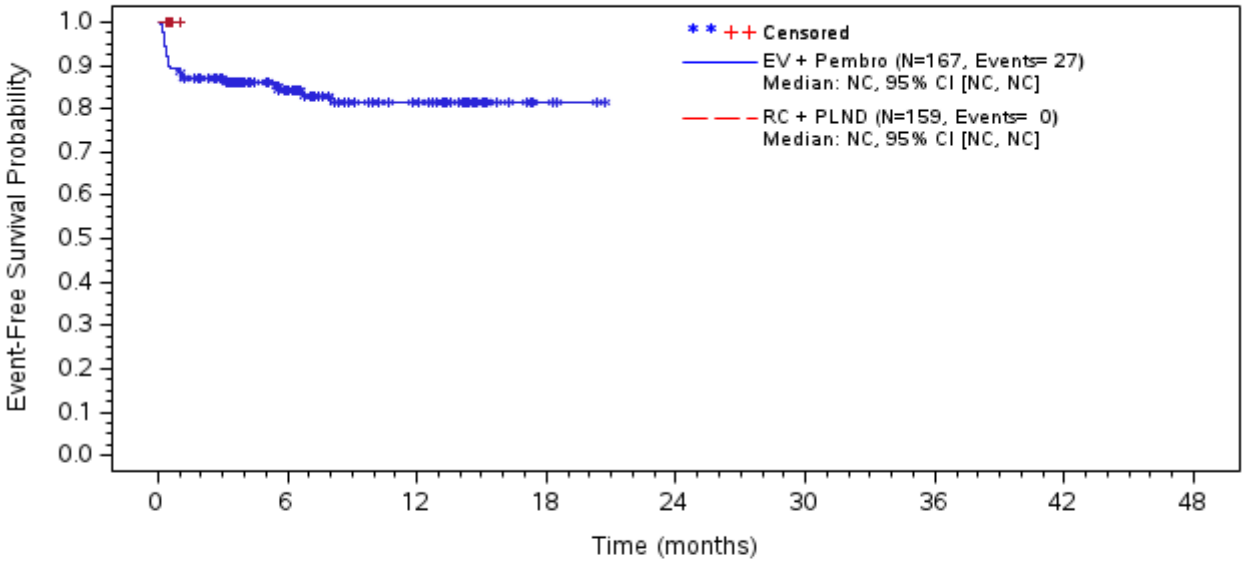
	# at Risk (% Censored)								
1	167 (0.0)	78 (29.9)	42 (49.7)	3 (73.1)	0 (74.9)	0 (74.9)	0 (74.9)	0 (74.9)	0 (74.9)
3	159 (0.0)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.65.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Rash Maculo-Papular (PT) - SAF2 Analysis Set



at Risk (% Censored)

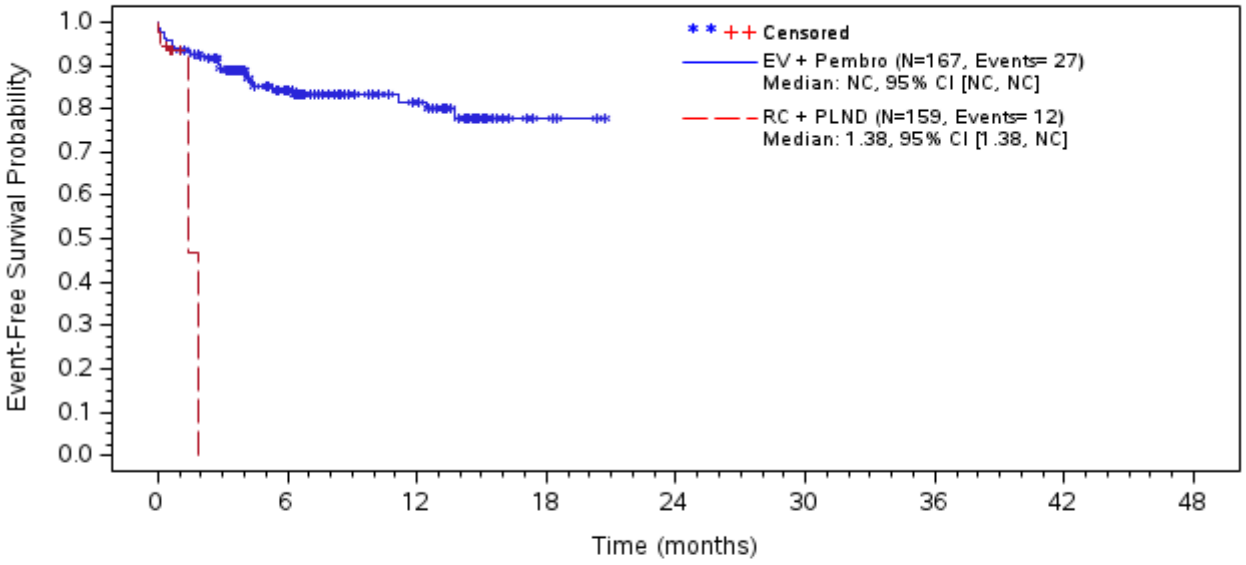
1	167 (0.0)	80 (37.1)	51 (53.3)	4 (81.4)	0 (83.8)	0 (83.8)	0 (83.8)	0 (83.8)	0 (83.8)
3	159 (0.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.66.1: Kaplan-Meier Plot of Time to Treatment Emergent Adverse Events in Combined Treatment Phases - Vascular Disorders (SOC) - SAF2 Analysis Set



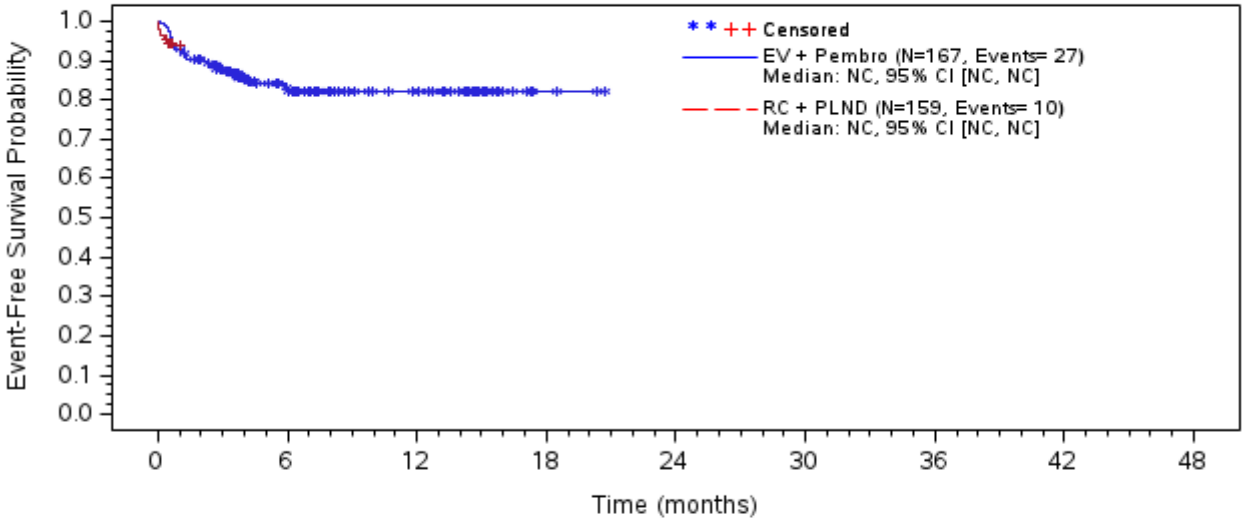
# at Risk (% Censored)									
1	167 (0.0)	85 (35.3)	50 (55.1)	4 (81.4)	0 (83.8)	0 (83.8)	0 (83.8)	0 (83.8)	0 (83.8)
3	159 (0.0)	0 (92.5)	0 (92.5)	0 (92.5)	0 (92.5)	0 (92.5)	0 (92.5)	0 (92.5)	0 (92.5)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.67.1: Kaplan-Meier Plot of Time to Severe Treatment Emergent Adverse Events in Combined Treatment Phases - Blood and Lymphatic System Disorders (SOC) - SAF2 Analysis Set



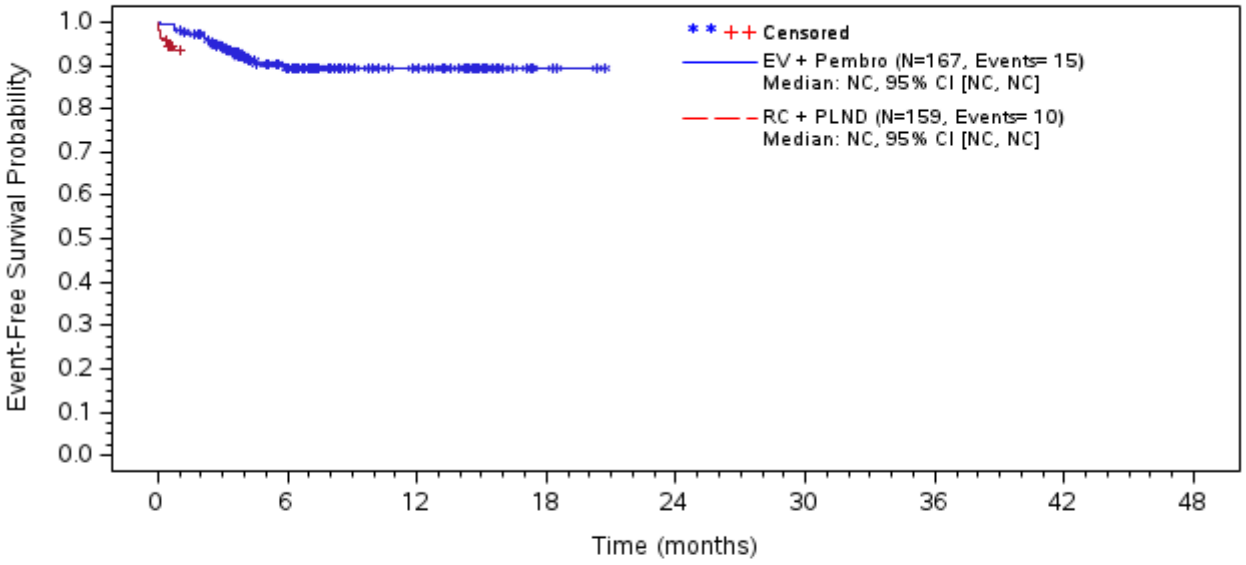
	# at Risk (% Censored)								
1	167 (0.0)	83 (34.7)	51 (53.3)	3 (82.0)	0 (83.8)	0 (83.8)	0 (83.8)	0 (83.8)	0 (83.8)
3	159 (0.0)	0 (93.7)	0 (93.7)	0 (93.7)	0 (93.7)	0 (93.7)	0 (93.7)	0 (93.7)	0 (93.7)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.68.1: Kaplan-Meier Plot of Time to Severe Treatment Emergent Adverse Events in Combined Treatment Phases - Anaemia (PT) - SAF2 Analysis Set



at Risk (% Censored)

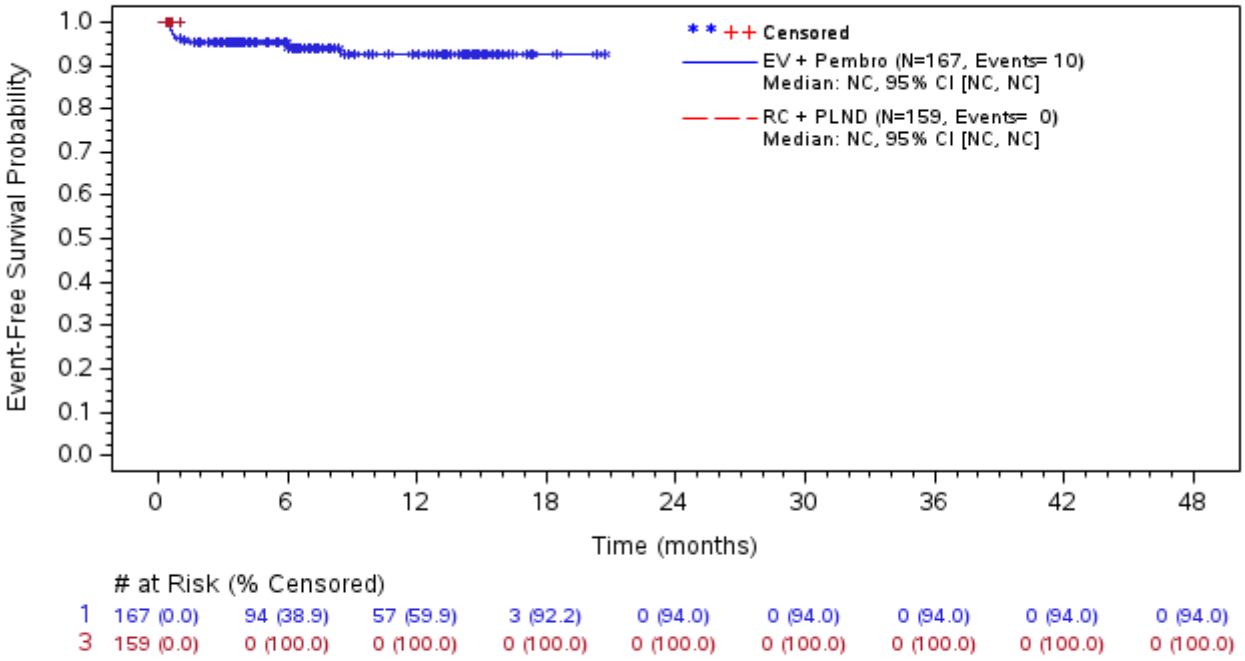
1	167 (0.0)	88 (38.3)	53 (59.3)	4 (88.6)	0 (91.0)	0 (91.0)	0 (91.0)	0 (91.0)	0 (91.0)
3	159 (0.0)	0 (93.7)	0 (93.7)	0 (93.7)	0 (93.7)	0 (93.7)	0 (93.7)	0 (93.7)	0 (93.7)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.69.1: Kaplan-Meier Plot of Time to Severe Treatment Emergent Adverse Events in Combined Treatment Phases - Neutropenia (PT) - SAF2 Analysis Set



at Risk (% Censored)

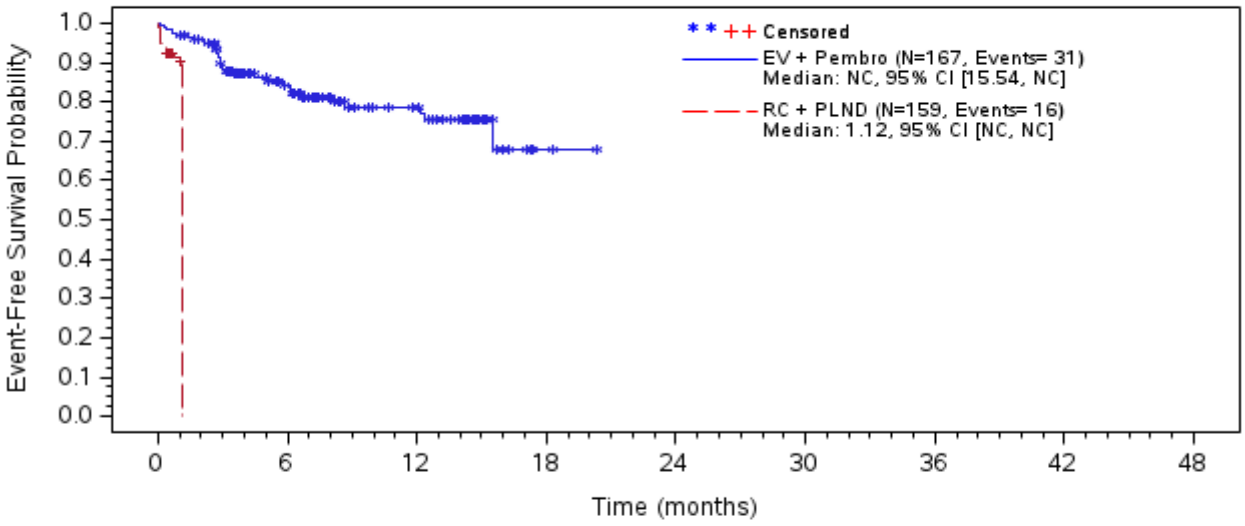
1	167 (0.0)	94 (38.9)	57 (59.9)	3 (92.2)	0 (94.0)	0 (94.0)	0 (94.0)	0 (94.0)	0 (94.0)
3	159 (0.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.70.1: Kaplan-Meier Plot of Time to Severe Treatment Emergent Adverse Events in Combined Treatment Phases - Gastrointestinal Disorders (SOC) - SAF2 Analysis Set



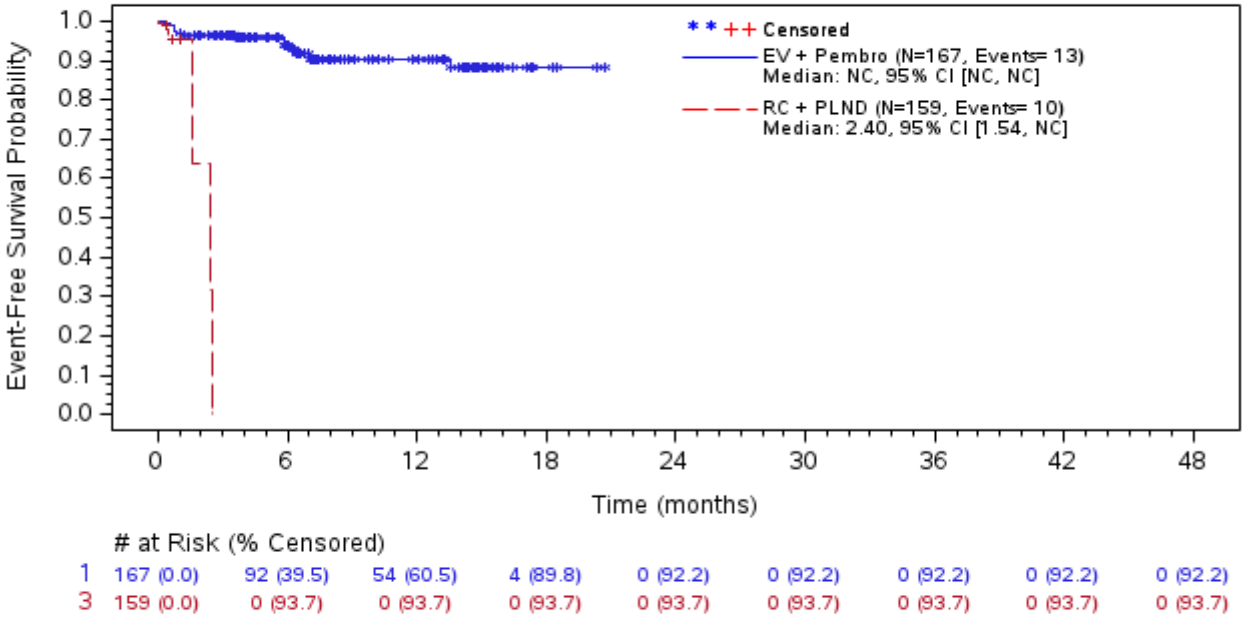
	# at Risk (% Censored)								
1	167 (0.0)	87 (34.1)	52 (52.1)	2 (80.2)	0 (81.4)	0 (81.4)	0 (81.4)	0 (81.4)	0 (81.4)
3	159 (0.0)	0 (89.9)	0 (89.9)	0 (89.9)	0 (89.9)	0 (89.9)	0 (89.9)	0 (89.9)	0 (89.9)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.71.1: Kaplan-Meier Plot of Time to Severe Treatment Emergent Adverse Events in Combined Treatment Phases - General Disorders and Administration Site Conditions (SOC) - SAF2 Analysis Set



at Risk (% Censored)

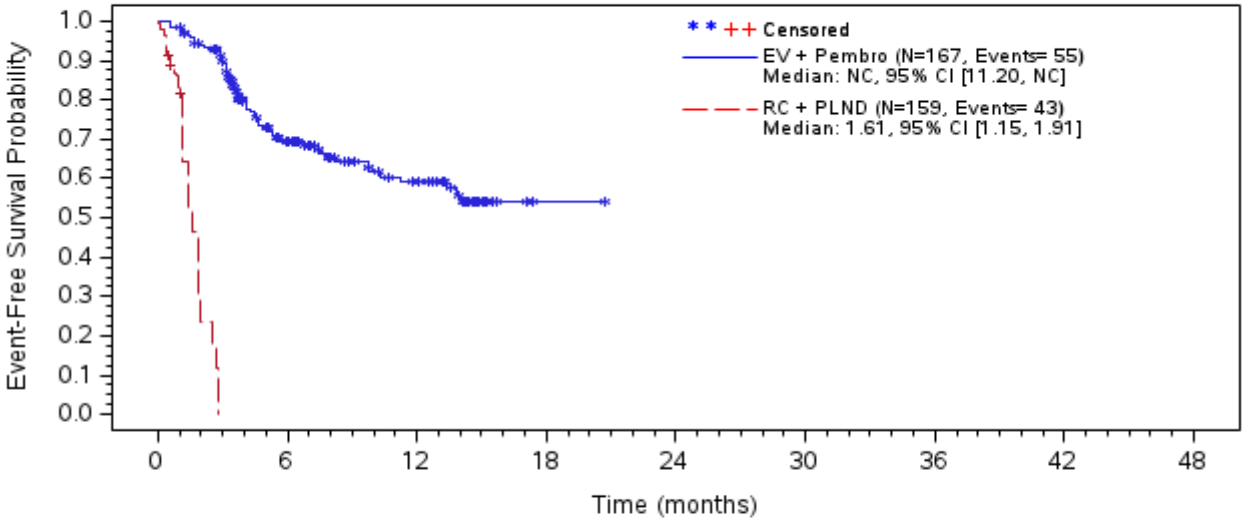
1	167 (0.0)	92 (39.5)	54 (60.5)	4 (89.8)	0 (92.2)	0 (92.2)	0 (92.2)	0 (92.2)	0 (92.2)
3	159 (0.0)	0 (93.7)	0 (93.7)	0 (93.7)	0 (93.7)	0 (93.7)	0 (93.7)	0 (93.7)	0 (93.7)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.72.1: Kaplan-Meier Plot of Time to Severe Treatment Emergent Adverse Events in Combined Treatment Phases - Infections and Infestations (SOC) - SAF2 Analysis Set



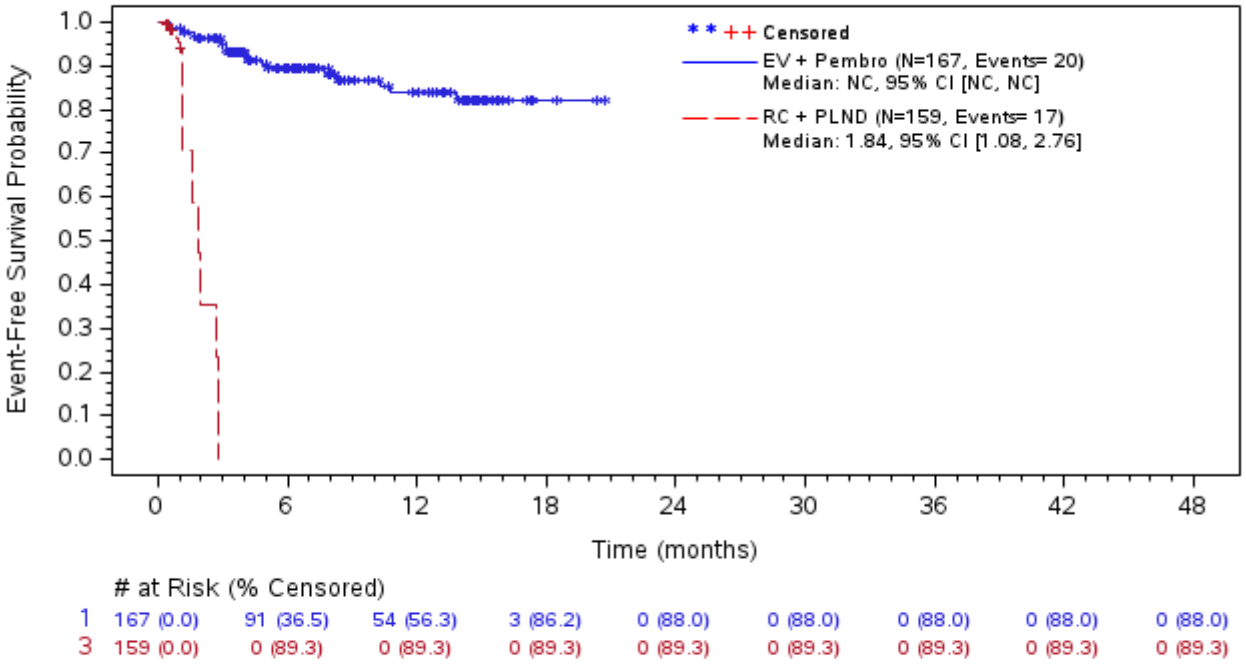
	# at Risk (% Censored)								
1	167 (0.0)	78 (27.5)	44 (42.5)	1 (66.5)	0 (67.1)	0 (67.1)	0 (67.1)	0 (67.1)	0 (67.1)
3	159 (0.0)	0 (73.0)	0 (73.0)	0 (73.0)	0 (73.0)	0 (73.0)	0 (73.0)	0 (73.0)	0 (73.0)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.73.1: Kaplan-Meier Plot of Time to Severe Treatment Emergent Adverse Events in Combined Treatment Phases - Urinary Tract Infection (PT) - SAF2 Analysis Set



at Risk (% Censored)

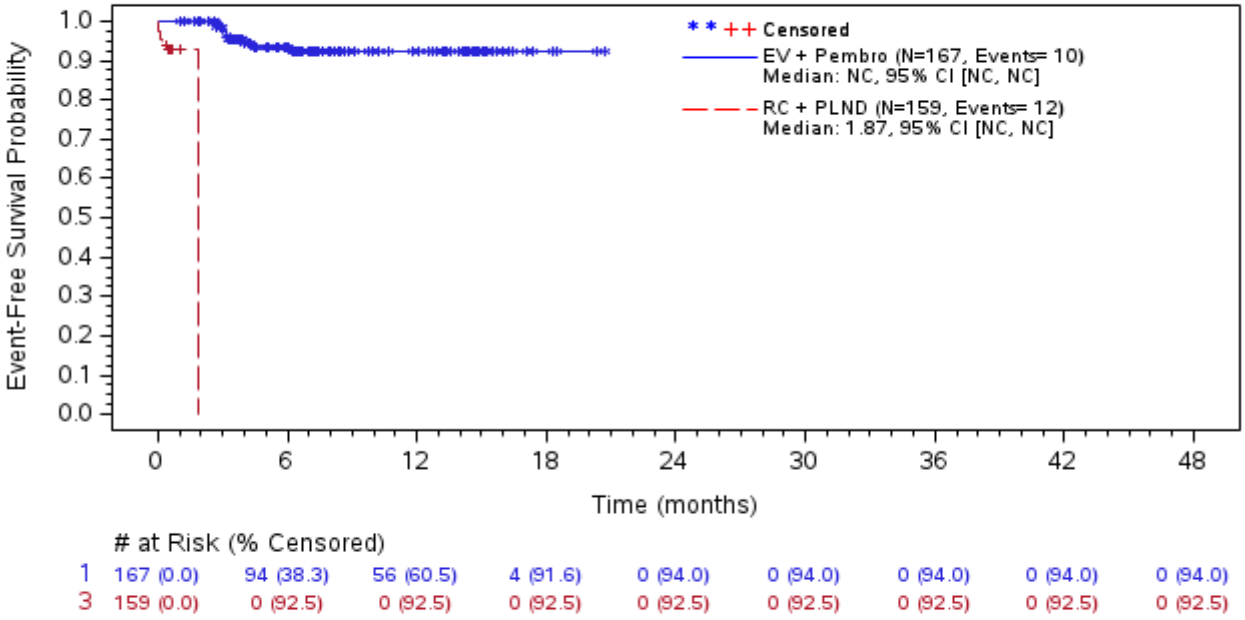
1	167 (0.0)	91 (36.5)	54 (56.3)	3 (86.2)	0 (88.0)	0 (88.0)	0 (88.0)	0 (88.0)	0 (88.0)
3	159 (0.0)	0 (89.3)	0 (89.3)	0 (89.3)	0 (89.3)	0 (89.3)	0 (89.3)	0 (89.3)	0 (89.3)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.74.1: Kaplan-Meier Plot of Time to Severe Treatment Emergent Adverse Events in Combined Treatment Phases - Injury, Poisoning and Procedural Complications (SOC) - SAF2 Analysis Set



at Risk (% Censored)

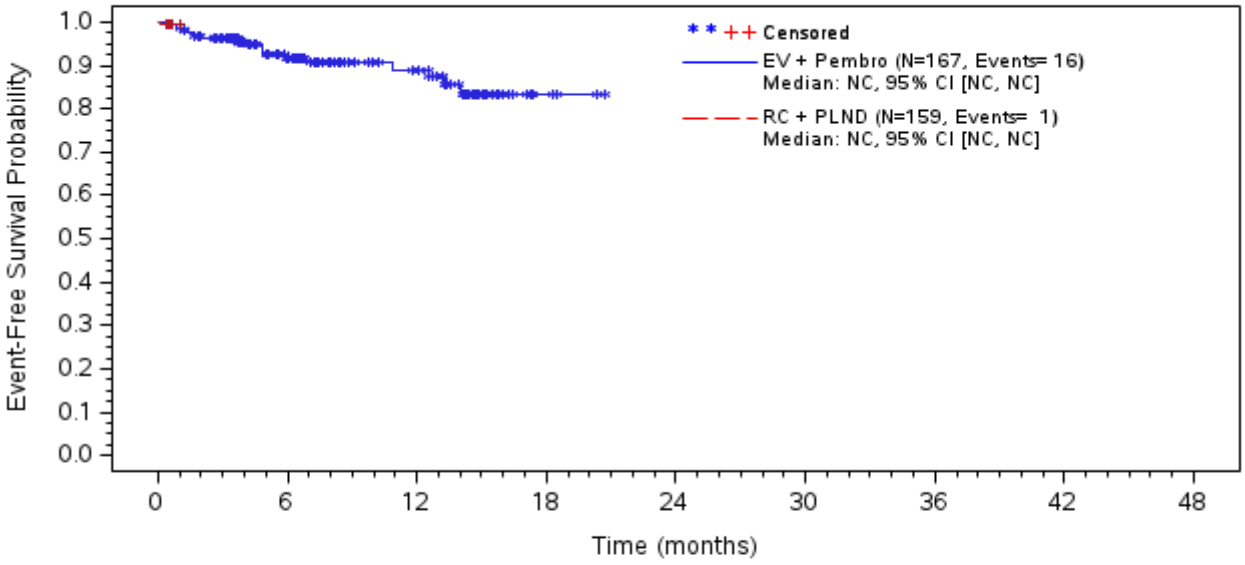
1	167 (0.0)	94 (38.3)	56 (60.5)	4 (91.6)	0 (94.0)	0 (94.0)	0 (94.0)	0 (94.0)	0 (94.0)
3	159 (0.0)	0 (92.5)	0 (92.5)	0 (92.5)	0 (92.5)	0 (92.5)	0 (92.5)	0 (92.5)	0 (92.5)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.75.1: Kaplan-Meier Plot of Time to Severe Treatment Emergent Adverse Events in Combined Treatment Phases - Investigations (SOC) - SAF2 Analysis Set



at Risk (% Censored)

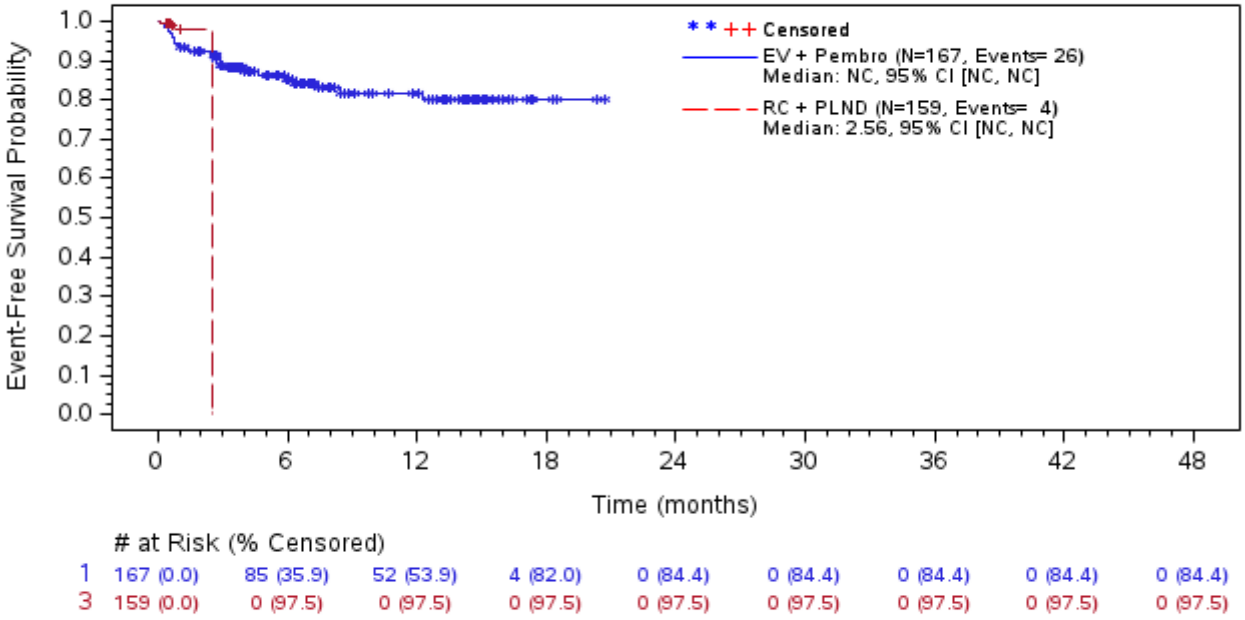
1	167 (0.0)	91 (38.9)	55 (59.3)	4 (88.0)	0 (90.4)	0 (90.4)	0 (90.4)	0 (90.4)	0 (90.4)
3	159 (0.0)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)	0 (99.4)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.76.1: Kaplan-Meier Plot of Time to Severe Treatment Emergent Adverse Events in Combined Treatment Phases - Metabolism and Nutrition Disorders (SOC) - SAF2 Analysis Set



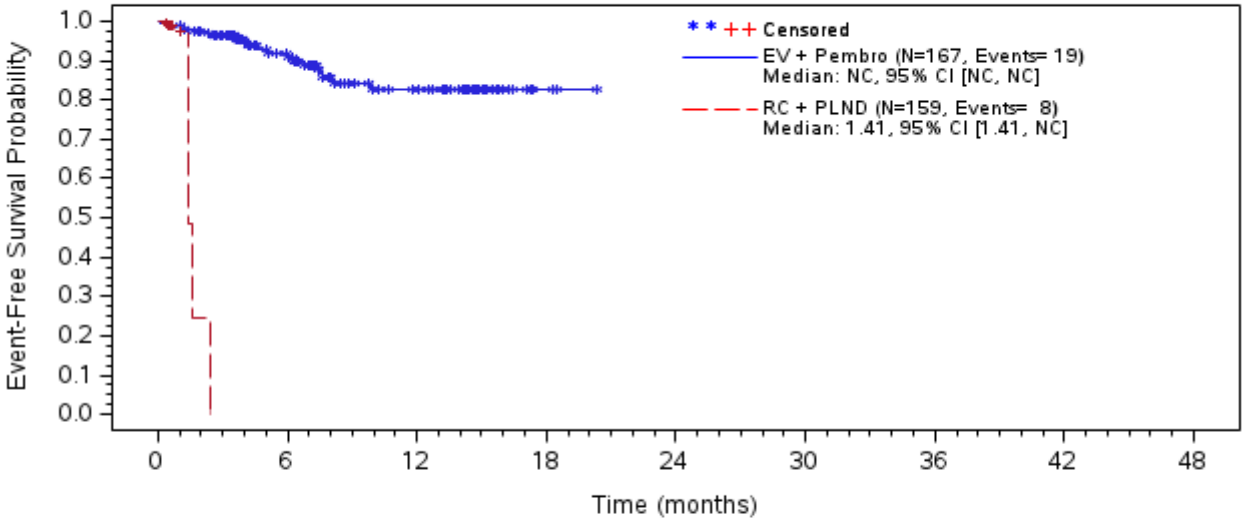
	# at Risk (% Censored)								
1	167 (0.0)	85 (35.9)	52 (53.9)	4 (82.0)	0 (84.4)	0 (84.4)	0 (84.4)	0 (84.4)	0 (84.4)
3	159 (0.0)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.77.1: Kaplan-Meier Plot of Time to Severe Treatment Emergent Adverse Events in Combined Treatment Phases - Renal and Urinary Disorders (SOC) - SAF2 Analysis Set



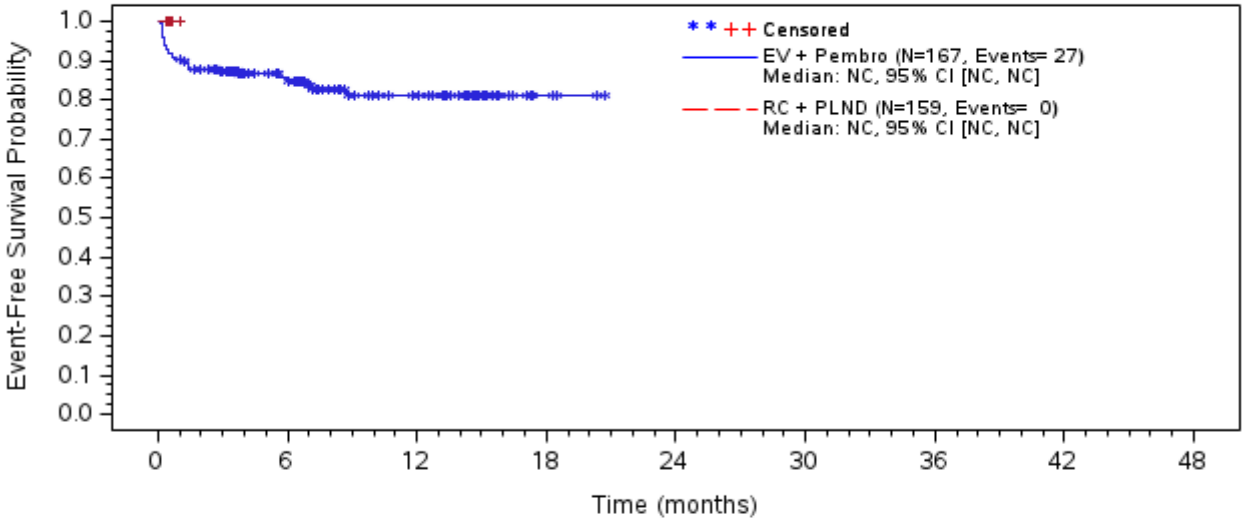
	# at Risk (% Censored)								
1	167 (0.0)	95 (36.5)	55 (55.7)	3 (86.8)	0 (88.6)	0 (88.6)	0 (88.6)	0 (88.6)	0 (88.6)
3	159 (0.0)	0 (95.0)	0 (95.0)	0 (95.0)	0 (95.0)	0 (95.0)	0 (95.0)	0 (95.0)	0 (95.0)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.78.1: Kaplan-Meier Plot of Time to Severe Treatment Emergent Adverse Events in Combined Treatment Phases - Skin and Subcutaneous Tissue Disorders (SOC) - SAF2 Analysis Set



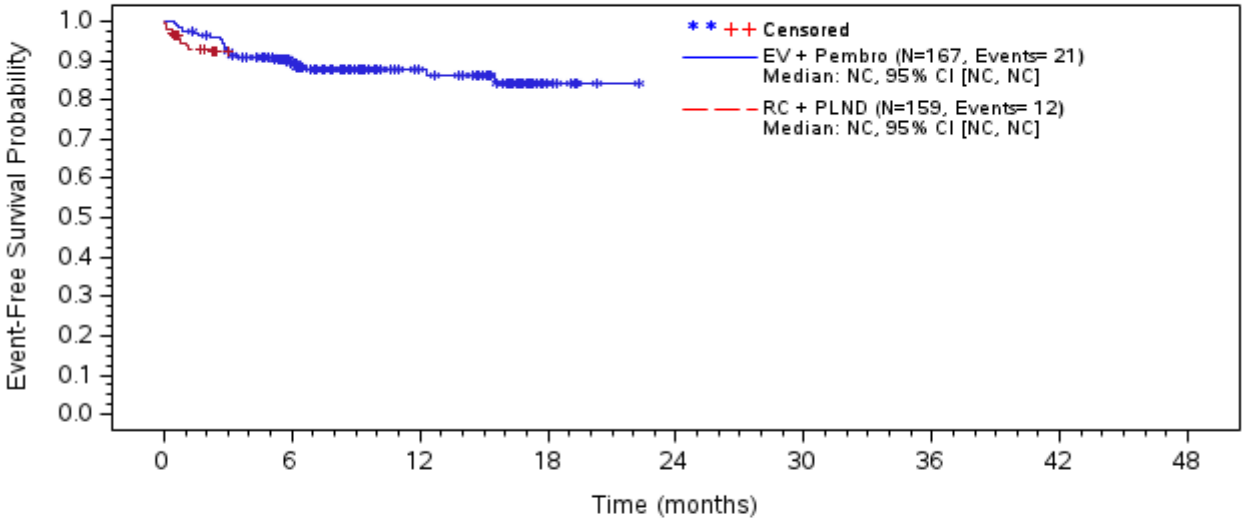
	# at Risk (% Censored)								
1	167 (0.0)	88 (32.9)	54 (51.5)	4 (81.4)	0 (83.8)	0 (83.8)	0 (83.8)	0 (83.8)	0 (83.8)
3	159 (0.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.79.1: Kaplan-Meier Plot of Time to Treatment Emergent Serious Adverse Events in Combined Treatment Phases - Gastrointestinal Disorders (SOC) - SAF2 Analysis Set



at Risk (% Censored)

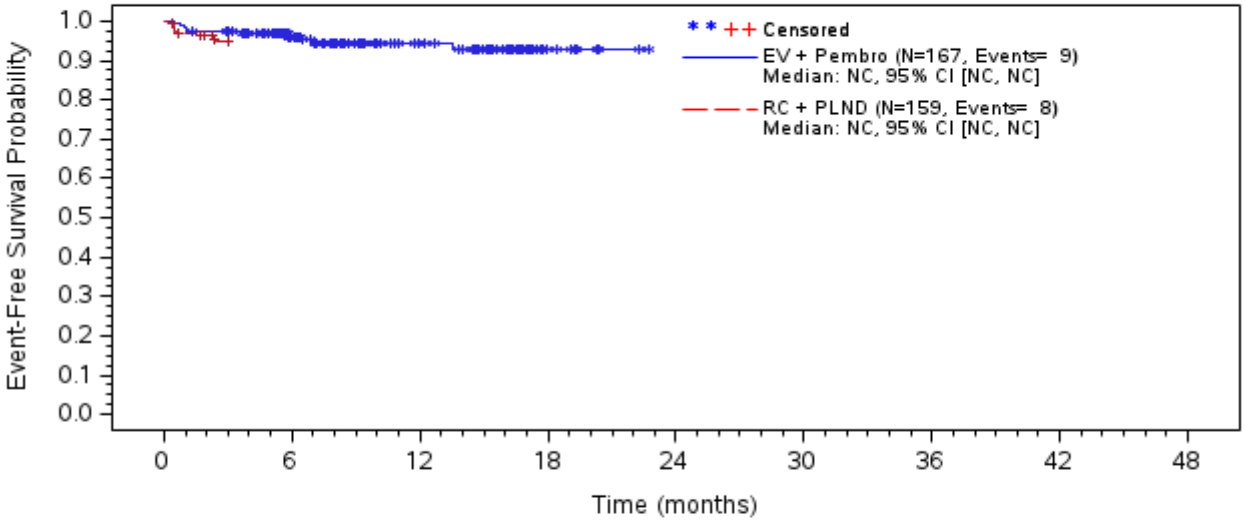
1	167 (0.0)	103 (28.1)	59 (53.3)	8 (82.6)	0 (87.4)	0 (87.4)	0 (87.4)	0 (87.4)	0 (87.4)
3	159 (0.0)	0 (92.5)	0 (92.5)	0 (92.5)	0 (92.5)	0 (92.5)	0 (92.5)	0 (92.5)	0 (92.5)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.80.1: Kaplan-Meier Plot of Time to Treatment Emergent Serious Adverse Events in Combined Treatment Phases - General Disorders and Administration Site Conditions (SOC) - SAF2 Analysis Set



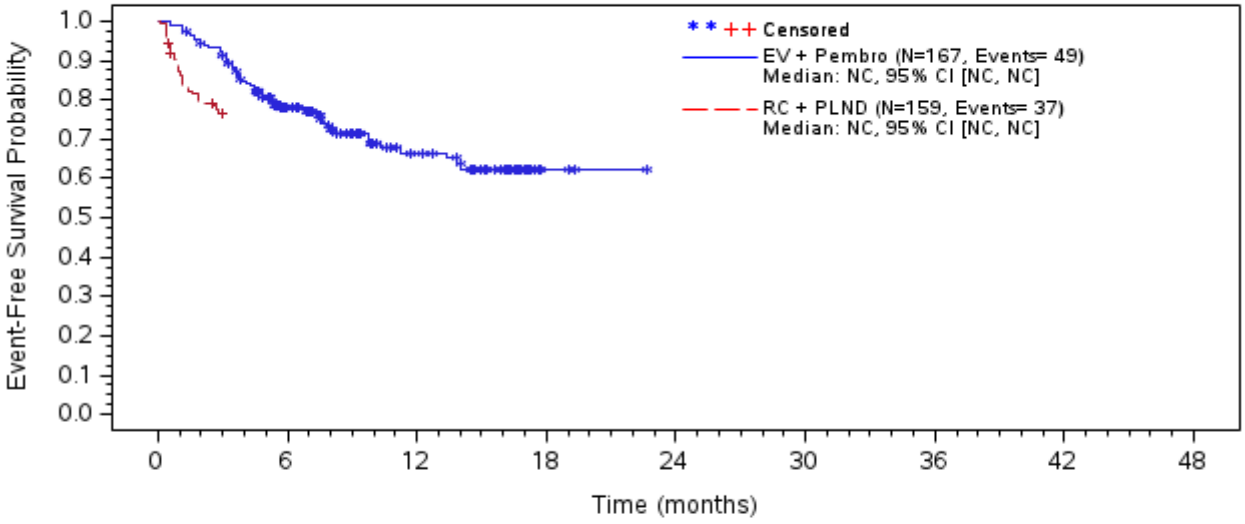
# at Risk (% Censored)									
1	167 (0.0)	107 (32.3)	61 (58.7)	9 (89.2)	0 (94.6)	0 (94.6)	0 (94.6)	0 (94.6)	0 (94.6)
3	159 (0.0)	0 (95.0)	0 (95.0)	0 (95.0)	0 (95.0)	0 (95.0)	0 (95.0)	0 (95.0)	0 (95.0)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.81.1: Kaplan-Meier Plot of Time to Treatment Emergent Serious Adverse Events in Combined Treatment Phases - Infections and Infestations (SOC) - SAF2 Analysis Set



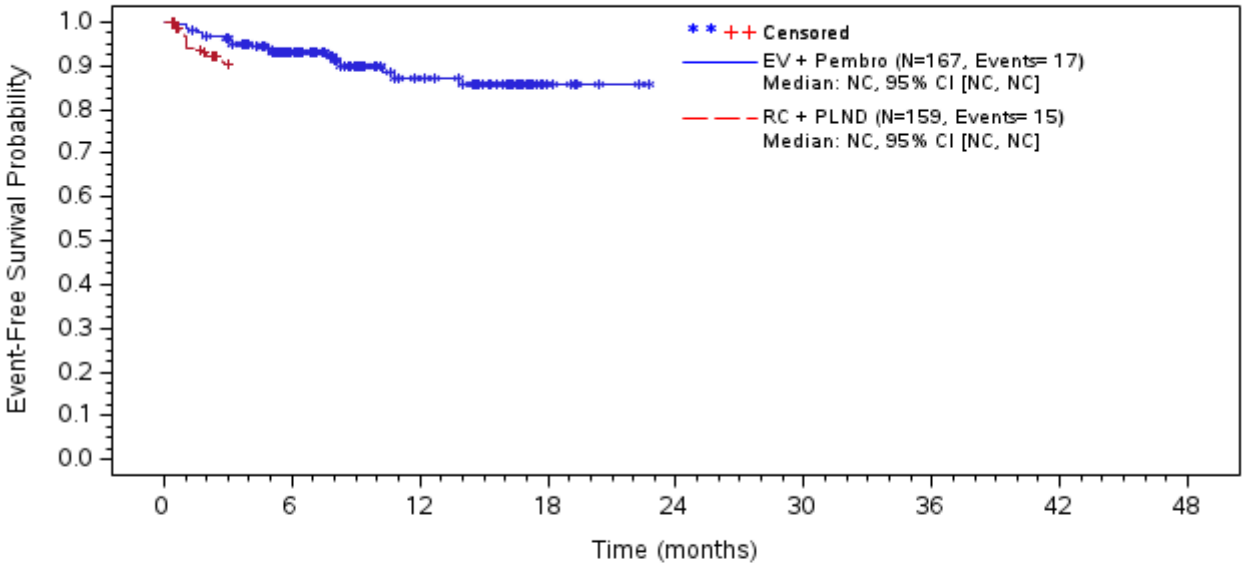
# at Risk (% Censored)									
1	167 (0.0)	92 (24.0)	49 (43.1)	3 (68.9)	0 (70.7)	0 (70.7)	0 (70.7)	0 (70.7)	0 (70.7)
3	159 (0.0)	0 (76.7)	0 (76.7)	0 (76.7)	0 (76.7)	0 (76.7)	0 (76.7)	0 (76.7)	0 (76.7)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.82.1: Kaplan-Meier Plot of Time to Treatment Emergent Serious Adverse Events in Combined Treatment Phases - Urinary Tract Infection (PT) - SAF2 Analysis Set



at Risk (% Censored)

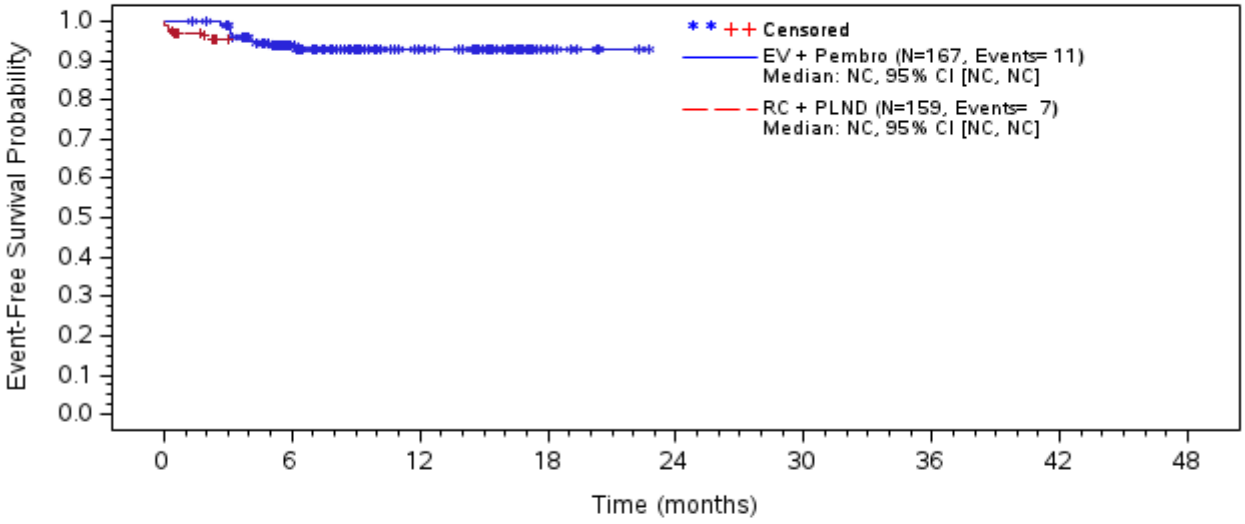
1	167 (0.0)	107 (29.3)	57 (56.3)	7 (85.6)	0 (89.8)	0 (89.8)	0 (89.8)	0 (89.8)	0 (89.8)
3	159 (0.0)	0 (90.6)	0 (90.6)	0 (90.6)	0 (90.6)	0 (90.6)	0 (90.6)	0 (90.6)	0 (90.6)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.83.1: Kaplan-Meier Plot of Time to Treatment Emergent Serious Adverse Events in Combined Treatment Phases - Injury, Poisoning and Procedural Complications (SOC) - SAF2 Analysis Set



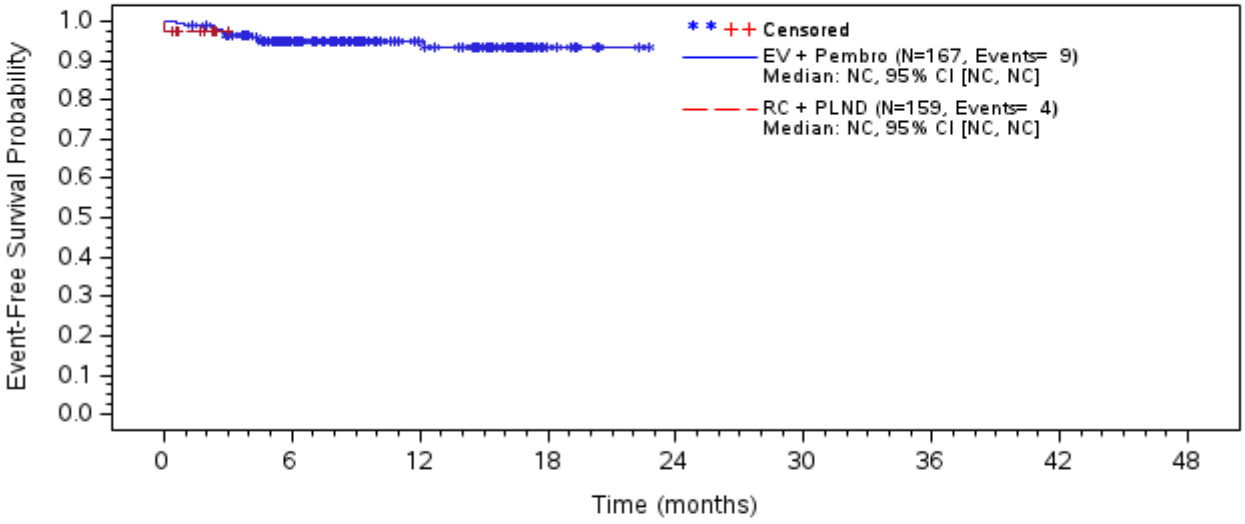
# at Risk (% Censored)									
1	167 (0.0)	105 (31.1)	60 (57.5)	8 (88.6)	0 (93.4)	0 (93.4)	0 (93.4)	0 (93.4)	0 (93.4)
3	159 (0.0)	0 (95.6)	0 (95.6)	0 (95.6)	0 (95.6)	0 (95.6)	0 (95.6)	0 (95.6)	0 (95.6)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.84.1: Kaplan-Meier Plot of Time to Treatment Emergent Serious Adverse Events in Combined Treatment Phases - Neoplasms Benign, Malignant and Unspecified (Incl Cysts and Polyps) (SOC) - SAF2 Analysis Set



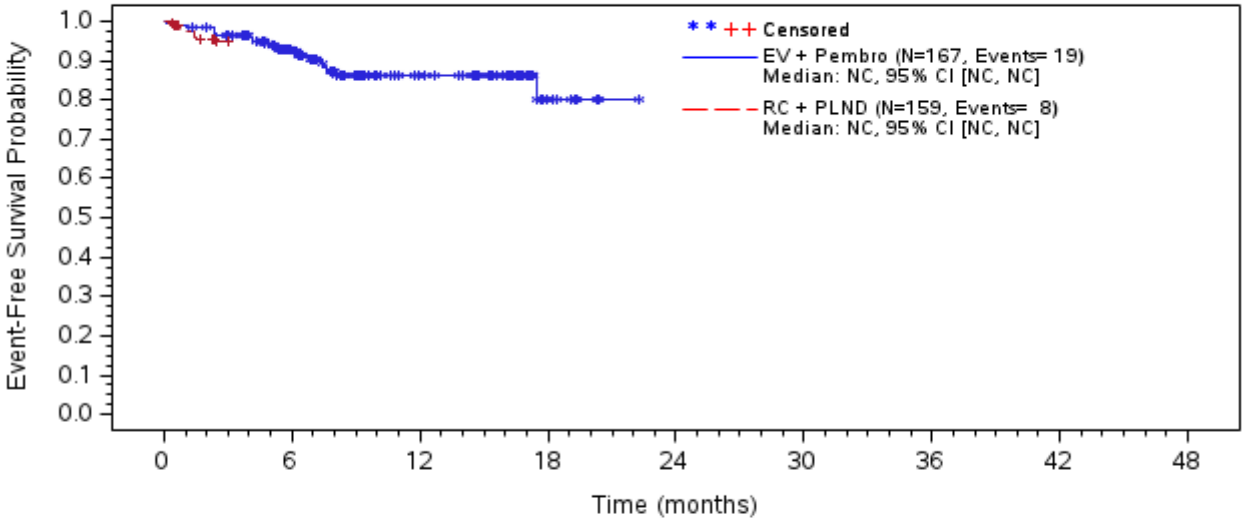
# at Risk (% Censored)									
1	167 (0.0)	108 (30.5)	61 (58.7)	9 (89.2)	0 (94.6)	0 (94.6)	0 (94.6)	0 (94.6)	0 (94.6)
3	159 (0.0)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)	0 (97.5)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.85.1: Kaplan-Meier Plot of Time to Treatment Emergent Serious Adverse Events in Combined Treatment Phases - Renal and Urinary Disorders (SOC) - SAF2 Analysis Set



at Risk (% Censored)

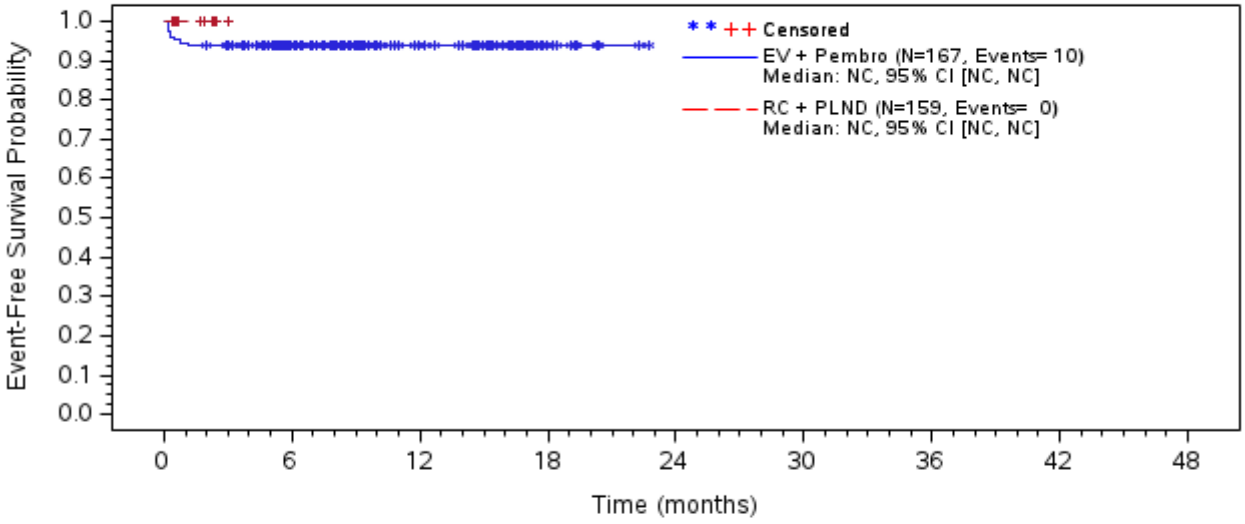
1	167 (0.0)	105 (30.5)	58 (54.5)	9 (83.2)	0 (88.6)	0 (88.6)	0 (88.6)	0 (88.6)	0 (88.6)
3	159 (0.0)	0 (95.0)	0 (95.0)	0 (95.0)	0 (95.0)	0 (95.0)	0 (95.0)	0 (95.0)	0 (95.0)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Figure 303.1.2001.86.1: Kaplan-Meier Plot of Time to Treatment Emergent Serious Adverse Events in Combined Treatment Phases - Skin and Subcutaneous Tissue Disorders (SOC) - SAF2 Analysis Set



at Risk (% Censored)

1	167 (0.0)	107 (29.9)	62 (56.9)	10 (88.0)	0 (94.0)	0 (94.0)	0 (94.0)	0 (94.0)	0 (94.0)
3	159 (0.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)	0 (100.0)

Abbreviations: # at Risk=number of patients at risk; CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.

Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.

ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Endpunkt: Unerwünschte Ereignisse; Binäre Analysen

Table 303.1.2002.1.1: Effect Measures of Proportion of Subjects with Treatment Emergent Adverse Events in Surgical Phase
SAF2 Analysis Set

	EV + Pembro (N=167)	RC + PLND (N=159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	99 (59.3%)	103 (64.8%)	
Number of patients without event	68 (40.7%)	56 (35.2%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			0.792 [0.505, 1.240]
Relative Risk (a)			
Unstratified RR, 95% CI			0.915 [0.772, 1.085]
Risk Difference (b)			
Unstratified RD, 95% CI			-0.055 [-0.160, 0.050]
Test on Differences (c)			
Unstratified p-value			0.3067

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.1.2: Effect Measures of Proportion of Subjects with Treatment Emergent Adverse Events in Surgical Phase by Subgroups
SAF2 Analysis Set

Subgroup	EV + Pembro		RC + PLND		EV + Pembro vs. RC + PLND				
	N	n (%)	N	n (%)	Unstratified RR, 95% CI (a)	Unstratified OR, 95% CI (a)	Unstratified RD, 95% CI (b)	Difference p-value (c)	Interaction p-value (d)
Cisplatin Eligibility									
Ineligible	138	82 (59.4)	129	85 (65.9)	0.902 [0.749, 1.086]	0.758 [0.461, 1.247]	-0.065 [-0.180, 0.051]	0.2750	0.7344
Eligible but Declined	29	17 (58.6)	30	18 (60.0)	0.977 [0.640, 1.491]	0.944 [0.334, 2.670]	-0.014 [-0.265, 0.237]	0.9141	
Tumor Stage									
T2N0	31	21 (67.7)	27	13 (48.1)	1.407 [0.888, 2.230]	2.262 [0.779, 6.569]	0.196 [-0.054, 0.446]	0.1307	0.0992
T3/T4aN0	129	74 (57.4)	125	86 (68.8)	0.834 [0.690, 1.008]	0.610 [0.365, 1.021]	-0.114 [-0.232, 0.003]	0.0591	
T1-4aN1	7	4 (57.1)	7	4 (57.1)	1.000 [0.404, 2.478]	1.000 [0.120, 8.306]	0.000 [-0.518, 0.518]	1.0000	
Geographical Regions									
US	21	16 (76.2)	23	18 (78.3)	0.974 [0.706, 1.343]	0.889 [0.217, 3.643]	-0.021 [-0.269, 0.227]	0.8700	0.8352
EU	76	50 (65.8)	69	48 (69.6)	0.946 [0.755, 1.184]	0.841 [0.419, 1.691]	-0.038 [-0.190, 0.114]	0.6276	
MOW	70	33 (47.1)	67	37 (55.2)	0.854 [0.615, 1.186]	0.723 [0.369, 1.417]	-0.081 [-0.248, 0.086]	0.3442	
Age Category									
< 65	29	20 (69.0)	28	16 (57.1)	1.207 [0.806, 1.806]	1.667 [0.563, 4.937]	0.118 [-0.131, 0.367]	0.3549	0.1344
>= 65	138	79 (57.2)	131	87 (66.4)	0.862 [0.714, 1.041]	0.677 [0.413, 1.111]	-0.092 [-0.207, 0.024]	0.1222	
Sex									
Male	135	77 (57.0)	120	77 (64.2)	0.889 [0.729, 1.084]	0.741 [0.447, 1.229]	-0.071 [-0.191, 0.048]	0.2453	0.4452
Female	32	22 (68.8)	39	26 (66.7)	1.031 [0.747, 1.423]	1.100 [0.404, 2.993]	0.021 [-0.198, 0.239]	0.8519	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; n=number of patients with events; NC=not calculated; OR=odds ratio; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy; RD=risk difference; RR=relative risk.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences; (d) Type 3 likelihood ratio test p-value from binominal regression model with log-link including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.2.1: Effect Measures of Proportion of Patients with Severe Treatment Emergent Adverse Events in Surgical Phase
SAF2 Analysis Set

	EV + Pembro (N=167)	RC + PLND (N=159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	53 (31.7%)	73 (45.9%)	
Number of patients without event	114 (68.3%)	86 (54.1%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			0.548 [0.349, 0.860]
Relative Risk (a)			
Unstratified RR, 95% CI			0.691 [0.523, 0.914]
Risk Difference (b)			
Unstratified RD, 95% CI			-0.142 [-0.247, -0.037]
Test on Differences (c)			
Unstratified p-value			0.0086

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.2.2: Effect Measures of Proportion of Patients with Severe Treatment Emergent Adverse Events in Surgical Phase by Subgroups
SAF2 Analysis Set

Subgroup	EV + Pembro		RC + PLND		EV + Pembro vs. RC + PLND				
	N	n (%)	N	n (%)	Unstratified RR, 95% CI (a)	Unstratified OR, 95% CI (a)	Unstratified RD, 95% CI (b)	Difference p-value (c)	Interaction p-value (d)
Cisplatin Eligibility									
Ineligible	138	47 (34.1)	129	65 (50.4)	0.676 [0.507, 0.902]	0.509 [0.311, 0.833]	-0.163 [-0.280, -0.046]	0.0069	0.7819
Eligible but Declined	29	6 (20.7)	30	8 (26.7)	0.776 [0.307, 1.961]	0.717 [0.214, 2.404]	-0.060 [-0.276, 0.157]	0.5895	
Tumor Stage									
T2N0	31	12 (38.7)	27	9 (33.3)	1.161 [0.581, 2.323]	1.263 [0.430, 3.713]	0.054 [-0.193, 0.301]	0.6709	0.2654
T3/T4aN0	129	39 (30.2)	125	61 (48.8)	0.620 [0.451, 0.851]	0.455 [0.272, 0.760]	-0.186 [-0.304, -0.068]	0.0025	
T1-4aN1	7	2 (28.6)	7	3 (42.9)	0.667 [0.156, 2.843]	0.533 [0.058, 4.912]	-0.143 [-0.639, 0.354]	0.7348	
Geographical Regions									
US	21	10 (47.6)	23	11 (47.8)	0.996 [0.536, 1.849]	0.992 [0.303, 3.242]	-0.002 [-0.298, 0.293]	0.9890	0.4105
EU	76	23 (30.3)	69	35 (50.7)	0.597 [0.395, 0.902]	0.422 [0.214, 0.832]	-0.205 [-0.361, -0.048]	0.0120	
MOW	70	20 (28.6)	67	27 (40.3)	0.709 [0.443, 1.136]	0.593 [0.291, 1.208]	-0.117 [-0.275, 0.041]	0.1484	
Age Category									
< 65	29	10 (34.5)	28	11 (39.3)	0.878 [0.444, 1.734]	0.813 [0.277, 2.390]	-0.048 [-0.298, 0.202]	0.7071	0.4537
>= 65	138	43 (31.2)	131	62 (47.3)	0.658 [0.484, 0.895]	0.504 [0.306, 0.828]	-0.162 [-0.277, -0.046]	0.0066	
Sex									
Male	135	39 (28.9)	120	52 (43.3)	0.667 [0.477, 0.932]	0.531 [0.316, 0.892]	-0.144 [-0.262, -0.027]	0.0163	0.5170
Female	32	14 (43.8)	39	21 (53.8)	0.813 [0.498, 1.324]	0.667 [0.260, 1.707]	-0.101 [-0.333, 0.131]	0.3972	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; n=number of patients with events; NC=not calculated; OR=odds ratio; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy; RD=risk difference; RR=relative risk.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences; (d) Type 3 likelihood ratio test p-value from binominal regression model with log-link including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.3.1: Effect Measures of Proportion of Patients with Treatment Emergent Serious Adverse Events in Surgical Phase
SAF2 Analysis Set

	EV + Pembro (N=167)	RC + PLND (N=159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	43 (25.7%)	65 (40.9%)	
Number of patients without event	124 (74.3%)	94 (59.1%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			0.501 [0.314, 0.802]
Relative Risk (a)			
Unstratified RR, 95% CI			0.630 [0.458, 0.866]
Risk Difference (b)			
Unstratified RD, 95% CI			-0.151 [-0.252, -0.050]
Test on Differences (c)			
Unstratified p-value			0.0037

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.3.2: Effect Measures of Proportion of Patients with Treatment Emergent Serious Adverse Events in Surgical Phase by Subgroups
SAF2 Analysis Set

Subgroup	EV + Pembro		RC + PLND		EV + Pembro vs. RC + PLND				
	N	n (%)	N	n (%)	Unstratified RR, 95% CI (a)	Unstratified OR, 95% CI (a)	Unstratified RD, 95% CI (b)	Difference p-value (c)	Interaction p-value (d)
Cisplatin Eligibility									
Ineligible	138	38 (27.5)	129	57 (44.2)	0.623 [0.447, 0.869]	0.480 [0.288, 0.799]	-0.166 [-0.280, -0.053]	0.0045	0.9452
Eligible but Declined	29	5 (17.2)	30	8 (26.7)	0.647 [0.239, 1.747]	0.573 [0.163, 2.016]	-0.094 [-0.304, 0.115]	0.3825	
Tumor Stage									
T2N0	31	8 (25.8)	27	8 (29.6)	0.871 [0.379, 2.004]	0.826 [0.261, 2.617]	-0.038 [-0.269, 0.193]	0.7452	0.5893
T3/T4aN0	129	34 (26.4)	125	54 (43.2)	0.610 [0.429, 0.867]	0.471 [0.278, 0.798]	-0.168 [-0.284, -0.053]	0.0048	
T1-4aN1	7	1 (14.3)	7	3 (42.9)	0.333 [0.045, 2.478]	0.222 [0.017, 2.970]	-0.286 [-0.735, 0.163]	0.3097	
Geographical Regions									
US	21	6 (28.6)	23	11 (47.8)	0.597 [0.269, 1.329]	0.436 [0.125, 1.525]	-0.193 [-0.474, 0.089]	0.1901	0.9667
EU	76	21 (27.6)	69	31 (44.9)	0.615 [0.393, 0.963]	0.468 [0.234, 0.934]	-0.173 [-0.327, -0.018]	0.0301	
MOW	70	16 (22.9)	67	23 (34.3)	0.666 [0.387, 1.146]	0.567 [0.267, 1.202]	-0.115 [-0.265, 0.036]	0.1369	
Age Category									
< 65	29	10 (34.5)	28	12 (42.9)	0.805 [0.416, 1.556]	0.702 [0.241, 2.047]	-0.084 [-0.336, 0.168]	0.5162	0.4263
>= 65	138	33 (23.9)	131	53 (40.5)	0.591 [0.411, 0.850]	0.463 [0.274, 0.781]	-0.165 [-0.276, -0.055]	0.0036	
Sex									
Male	135	34 (25.2)	120	46 (38.3)	0.657 [0.454, 0.950]	0.542 [0.317, 0.925]	-0.131 [-0.245, -0.018]	0.0239	0.7294
Female	32	9 (28.1)	39	19 (48.7)	0.577 [0.304, 1.096]	0.412 [0.152, 1.113]	-0.206 [-0.427, 0.015]	0.0773	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; n=number of patients with events; NC=not calculated; OR=odds ratio; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy; RD=risk difference; RR=relative risk.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences; (d) Type 3 likelihood ratio test p-value from binominal regression model with log-link including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.4.1: Effect Measures of Proportion of Patients with Treatment Emergent Adverse Events leading to Treatment Discontinuation in Surgical Phase SAF2 Analysis Set

	EV + Pembro (N=167)	**RC + PLND (N=159)**	**EV + Pembro vs. RC + PLND**
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	5 (3.0%)	0 (0.0%)	
Number of patients without event	162 (97.0%)	159 (100.0%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			10.797 [0.592, 196.87]
Relative Risk (a)			
Unstratified RR, 95% CI			10.476 [0.584, 187.93]
Risk Difference (b)			
Unstratified RD, 95% CI			0.030 [0.004, 0.056]
Test on Differences (c)			
Unstratified p-value			0.0291

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.4.2: Effect Measures of Proportion of Patients with Treatment Emergent Adverse Events leading to Treatment Discontinuation in Surgical Phase by Subgroups
SAF2 Analysis Set

Subgroup	EV + Pembro		RC + PLND		EV + Pembro vs. RC + PLND				
	N	n (%)	N	n (%)	Unstratified RR, 95% CI (a)	Unstratified OR, 95% CI (a)	Unstratified RD, 95% CI (b)	Difference p-value (c)	Interaction p-value (d)
Cisplatin Eligibility									
Ineligible	138	4 (2.9)	129	0 (0.0)	8.417 [0.458, 154.81]	8.665 [0.462, 162.56]	0.029 [0.001, 0.057]	0.0538	NC
Eligible but Declined	29	1 (3.4)	30	0 (0.0)	3.100 [0.131, 73.142]	3.211 [0.126, 82.066]	0.034 [-0.032, 0.101]	0.3616	
Tumor Stage									
T2N0	31	1 (3.2)	27	0 (0.0)	2.625 [0.111, 61.883]	2.705 [0.106, 69.194]	0.032 [-0.030, 0.094]	0.5146	NC
T3/T4aN0	129	4 (3.1)	125	0 (0.0)	8.723 [0.475, 160.36]	9.000 [0.480, 168.92]	0.031 [0.001, 0.061]	0.0516	
T1-4aN1	7	0 (0.0)	7	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC [NC, NC]	NC	
Geographical Regions									
US	21	1 (4.8)	23	0 (0.0)	3.273 [0.141, 76.212]	3.439 [0.133, 89.134]	0.048 [-0.043, 0.139]	0.3549	NC
EU	76	2 (2.6)	69	0 (0.0)	4.545 [0.222, 93.055]	4.664 [0.220, 98.876]	0.026 [-0.010, 0.062]	0.2226	
MOW	70	2 (2.9)	67	0 (0.0)	4.789 [0.234, 97.941]	4.927 [0.232, 104.55]	0.029 [-0.010, 0.068]	0.2234	
Age Category									
< 65	29	1 (3.4)	28	0 (0.0)	2.900 [0.123, 68.331]	3.000 [0.117, 76.789]	0.034 [-0.032, 0.101]	0.5272	NC
>= 65	138	4 (2.9)	131	0 (0.0)	8.547 [0.465, 157.21]	8.799 [0.469, 165.06]	0.029 [0.001, 0.057]	0.0539	
Sex									
Male	135	4 (3.0)	120	0 (0.0)	8.007 [0.436, 147.20]	8.247 [0.439, 154.79]	0.030 [0.001, 0.058]	0.0593	1.0000
Female	32	1 (3.1)	39	0 (0.0)	3.636 [0.153, 86.335]	3.762 [0.148, 95.545]	0.031 [-0.029, 0.092]	0.3517	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; n=number of patients with events; NC=not calculated; OR=odds ratio; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; RC=radical cystectomy; RD=risk difference; RR=relative risk.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences; (d) Type 3 likelihood ratio test p-value from binominal regression model with log-link including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.5.1: Effect Measures of Proportion of Subjects with Treatment Emergent Adverse Events in Surgical Phase - Blood and Lymphatic System Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N=167)	RC + PLND (N=159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	20 (12.0%)	19 (11.9%)	
Number of patients without event	147 (88.0%)	140 (88.1%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			1.003 [0.513, 1.958]
Relative Risk (a)			
Unstratified RR, 95% CI			1.002 [0.556, 1.806]
Risk Difference (b)			
Unstratified RD, 95% CI			0.000 [-0.070, 0.071]
Test on Differences (c)			
Unstratified p-value			0.9942

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.6.1: Effect Measures of Proportion of Subjects with Treatment Emergent Adverse Events in Surgical Phase - Anaemia (PT)
SAF2 Analysis Set

	EV + Pembro (N=167)	RC + PLND (N=159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	20 (12.0%)	19 (11.9%)	
Number of patients without event	147 (88.0%)	140 (88.1%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			1.003 [0.513, 1.958]
Relative Risk (a)			
Unstratified RR, 95% CI			1.002 [0.556, 1.806]
Risk Difference (b)			
Unstratified RD, 95% CI			0.000 [-0.070, 0.071]
Test on Differences (c)			
Unstratified p-value			0.9942

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.7.1: Effect Measures of Proportion of Subjects with Treatment Emergent Adverse Events in Surgical Phase - Gastrointestinal Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N=167)	RC + PLND (N=159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	39 (23.4%)	45 (28.3%)	
Number of patients without event	128 (76.6%)	114 (71.7%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			0.772 [0.469, 1.270]
Relative Risk (a)			
Unstratified RR, 95% CI			0.825 [0.570, 1.194]
Risk Difference (b)			
Unstratified RD, 95% CI			-0.049 [-0.144, 0.045]
Test on Differences (c)			
Unstratified p-value			0.3072

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.8.1: Effect Measures of Proportion of Subjects with Treatment Emergent Adverse Events in Surgical Phase - Constipation (PT)
SAF2 Analysis Set

	EV + Pembro (N=167)	RC + PLND (N=159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	11 (6.6%)	13 (8.2%)	
Number of patients without event	156 (93.4%)	146 (91.8%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			0.792 [0.344, 1.823]
Relative Risk (a)			
Unstratified RR, 95% CI			0.806 [0.372, 1.745]
Risk Difference (b)			
Unstratified RD, 95% CI			-0.016 [-0.073, 0.041]
Test on Differences (c)			
Unstratified p-value			0.5828

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.9.1: Effect Measures of Proportion of Subjects with Treatment Emergent Adverse Events in Surgical Phase - Nausea (PT)
SAF2 Analysis Set

	EV + Pembro (N=167)	RC + PLND (N=159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	9 (5.4%)	12 (7.5%)	
Number of patients without event	158 (94.6%)	147 (92.5%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			0.698 [0.286, 1.704]
Relative Risk (a)			
Unstratified RR, 95% CI			0.714 [0.309, 1.648]
Risk Difference (b)			
Unstratified RD, 95% CI			-0.022 [-0.075, 0.032]
Test on Differences (c)			
Unstratified p-value			0.4276

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.10.1: Effect Measures of Proportion of Subjects with Treatment Emergent Adverse Events in Surgical Phase - General Disorders and Administration Site Conditions (SOC)
SAF2 Analysis Set

	EV + Pembro (N=167)	**RC + PLND (N=159)**	**EV + Pembro vs. RC + PLND**
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	14 (8.4%)	22 (13.8%)	
Number of patients without event	153 (91.6%)	137 (86.2%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			0.570 [0.281, 1.157]
Relative Risk (a)			
Unstratified RR, 95% CI			0.606 [0.321, 1.142]
Risk Difference (b)			
Unstratified RD, 95% CI			-0.055 [-0.123, 0.014]
Test on Differences (c)			
Unstratified p-value			0.1164

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.11.1: Effect Measures of Proportion of Subjects with Treatment Emergent Adverse Events in Surgical Phase - Infections and Infestations (SOC)
SAF2 Analysis Set

	EV + Pembro (N=167)	RC + PLND (N=159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	36 (21.6%)	48 (30.2%)	
Number of patients without event	131 (78.4%)	111 (69.8%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			0.635 [0.385, 1.048]
Relative Risk (a)			
Unstratified RR, 95% CI			0.714 [0.491, 1.038]
Risk Difference (b)			
Unstratified RD, 95% CI			-0.086 [-0.181, 0.008]
Test on Differences (c)			
Unstratified p-value			0.0749

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.12.1: Effect Measures of Proportion of Subjects with Treatment Emergent Adverse Events in Surgical Phase - Urinary Tract Infection (PT)
SAF2 Analysis Set

	EV + Pembro (N=167)	RC + PLND (N=159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	13 (7.8%)	20 (12.6%)	
Number of patients without event	154 (92.2%)	139 (87.4%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			0.587 [0.281, 1.223]
Relative Risk (a)			
Unstratified RR, 95% CI			0.619 [0.319, 1.202]
Risk Difference (b)			
Unstratified RD, 95% CI			-0.048 [-0.114, 0.018]
Test on Differences (c)			
Unstratified p-value			0.1514

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.13.1: Effect Measures of Proportion of Subjects with Treatment Emergent Adverse Events in Surgical Phase - Injury, Poisoning and Procedural Complications (SOC)
SAF2 Analysis Set

	EV + Pembro (N=167)	RC + PLND (N=159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	26 (15.6%)	29 (18.2%)	
Number of patients without event	141 (84.4%)	130 (81.8%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			0.827 [0.463, 1.477]
Relative Risk (a)			
Unstratified RR, 95% CI			0.854 [0.527, 1.383]
Risk Difference (b)			
Unstratified RD, 95% CI			-0.027 [-0.108, 0.055]
Test on Differences (c)			
Unstratified p-value			0.5199

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.14.1: Effect Measures of Proportion of Subjects with Treatment Emergent Adverse Events in Surgical Phase - Procedural Pain (PT)
SAF2 Analysis Set

	EV + Pembro (N=167)	RC + PLND (N=159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	9 (5.4%)	12 (7.5%)	
Number of patients without event	158 (94.6%)	147 (92.5%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			0.698 [0.286, 1.704]
Relative Risk (a)			
Unstratified RR, 95% CI			0.714 [0.309, 1.648]
Risk Difference (b)			
Unstratified RD, 95% CI			-0.022 [-0.075, 0.032]
Test on Differences (c)			
Unstratified p-value			0.4276

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.15.1: Effect Measures of Proportion of Subjects with Treatment Emergent Adverse Events in Surgical Phase - Investigations (SOC)
SAF2 Analysis Set

	EV + Pembro (N=167)	RC + PLND (N=159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	9 (5.4%)	15 (9.4%)	
Number of patients without event	158 (94.6%)	144 (90.6%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			0.547 [0.232, 1.288]
Relative Risk (a)			
Unstratified RR, 95% CI			0.571 [0.257, 1.268]
Risk Difference (b)			
Unstratified RD, 95% CI			-0.040 [-0.097, 0.016]
Test on Differences (c)			
Unstratified p-value			0.1622

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.16.1: Effect Measures of Proportion of Subjects with Treatment Emergent Adverse Events in Surgical Phase - Metabolism and Nutrition Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N=167)	RC + PLND (N=159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	22 (13.2%)	19 (11.9%)	
Number of patients without event	145 (86.8%)	140 (88.1%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			1.118 [0.580, 2.155]
Relative Risk (a)			
Unstratified RR, 95% CI			1.102 [0.621, 1.957]
Risk Difference (b)			
Unstratified RD, 95% CI			0.012 [-0.060, 0.084]
Test on Differences (c)			
Unstratified p-value			0.7390

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.17.1: Effect Measures of Proportion of Subjects with Treatment Emergent Adverse Events in Surgical Phase - Neoplasms Benign, Malignant and Unspecified (Incl Cysts and Polyps) (SOC)
SAF2 Analysis Set

	EV + Pembro (N=167)	**RC + PLND (N=159)**	**EV + Pembro vs. RC + PLND**
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	18 (10.8%)	15 (9.4%)	
Number of patients without event	149 (89.2%)	144 (90.6%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			1.160 [0.563, 2.388]
Relative Risk (a)			
Unstratified RR, 95% CI			1.143 [0.597, 2.188]
Risk Difference (b)			
Unstratified RD, 95% CI			0.013 [-0.052, 0.079]
Test on Differences (c)			
Unstratified p-value			0.6875

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.18.1: Effect Measures of Proportion of Subjects with Treatment Emergent Adverse Events in Surgical Phase - Prostate Cancer (PT)
SAF2 Analysis Set

	EV + Pembro (N=167)	RC + PLND (N=159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	17 (10.2%)	15 (9.4%)	
Number of patients without event	150 (89.8%)	144 (90.6%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			1.088 [0.524, 2.260]
Relative Risk (a)			
Unstratified RR, 95% CI			1.079 [0.558, 2.087]
Risk Difference (b)			
Unstratified RD, 95% CI			0.007 [-0.057, 0.072]
Test on Differences (c)			
Unstratified p-value			0.8211

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.19.1: Effect Measures of Proportion of Subjects with Treatment Emergent Adverse Events in Surgical Phase - Nervous System Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N=167)	RC + PLND (N=159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	13 (7.8%)	4 (2.5%)	
Number of patients without event	154 (92.2%)	155 (97.5%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			3.271 [1.043, 10.255]
Relative Risk (a)			
Unstratified RR, 95% CI			3.094 [1.031, 9.290]
Risk Difference (b)			
Unstratified RD, 95% CI			0.053 [0.005, 0.100]
Test on Differences (c)			
Unstratified p-value			0.0336

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.19.2: Effect Measures of Proportion of Subjects with Treatment Emergent Adverse Events in Surgical Phase by Subgroups - Nervous System Disorders (SOC)
SAF2 Analysis Set

Subgroup	EV + Pembro		RC + PLND		EV + Pembro vs. RC + PLND				
	N	n (%)	N	n (%)	Unstratified RR, 95% CI (a)	Unstratified OR, 95% CI (a)	Unstratified RD, 95% CI (b)	Difference p-value (c)	Interaction p-value (d)
Cisplatin Eligibility									
Ineligible	138	8 (5.8)	129	4 (3.1)	1.870 [0.577, 6.060]	1.923 [0.565, 6.547]	0.027 [-0.022, 0.076]	0.3049	0.0559
Eligible but Declined	29	5 (17.2)	30	0 (0.0)	11.367 [0.657, 196.74]	13.694 [0.721, 259.94]	0.172 [0.035, 0.310]	0.0184	
Tumor Stage									
T2N0	31	2 (6.5)	27	1 (3.7)	1.742 [0.167, 18.162]	1.793 [0.153, 20.949]	0.027 [-0.085, 0.140]	0.7150	0.6719
T3/T4aN0	129	10 (7.8)	125	3 (2.4)	3.230 [0.910, 11.462]	3.417 [0.918, 12.725]	0.054 [0.000, 0.107]	0.0545	
T1-4aN1	7	1 (14.3)	7	0 (0.0)	3.000 [0.143, 63.149]	3.462 [0.119, 100.51]	0.143 [-0.116, 0.402]	0.5199	
Geographical Regions									
US	21	4 (19.0)	23	0 (0.0)	9.818 [0.560, 172.11]	12.086 [0.610, 239.51]	0.190 [0.023, 0.358]	0.0306	0.2131
EU	76	6 (7.9)	69	3 (4.3)	1.816 [0.472, 6.984]	1.886 [0.453, 7.849]	0.035 [-0.042, 0.113]	0.5308	
MOW	70	3 (4.3)	67	1 (1.5)	2.871 [0.306, 26.925]	2.955 [0.300, 29.141]	0.028 [-0.028, 0.084]	0.5289	
Age Category									
< 65	29	3 (10.3)	28	0 (0.0)	6.767 [0.365, 125.32]	7.528 [0.371, 152.73]	0.103 [-0.007, 0.214]	0.0996	0.1717
>= 65	138	10 (7.2)	131	4 (3.1)	2.373 [0.763, 7.381]	2.480 [0.758, 8.115]	0.042 [-0.010, 0.094]	0.1284	
Sex									
Male	135	11 (8.1)	120	3 (2.5)	3.259 [0.931, 11.407]	3.460 [0.942, 12.712]	0.056 [0.003, 0.110]	0.0523	0.8326
Female	32	2 (6.3)	39	1 (2.6)	2.437 [0.231, 25.674]	2.533 [0.219, 29.290]	0.037 [-0.061, 0.134]	0.5899	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; n=number of patients with events; NC=not calculated; OR=odds ratio; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; RD=risk difference; RR=relative risk; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences; (d) Type 3 likelihood ratio test p-value from binominal regression model with log-link including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.20.1: Effect Measures of Proportion of Subjects with Treatment Emergent Adverse Events in Surgical Phase - Psychiatric Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N=167)	RC + PLND (N=159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	7 (4.2%)	10 (6.3%)	
Number of patients without event	160 (95.8%)	149 (93.7%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			0.652 [0.242, 1.757]
Relative Risk (a)			
Unstratified RR, 95% CI			0.666 [0.260, 1.708]
Risk Difference (b)			
Unstratified RD, 95% CI			-0.021 [-0.069, 0.027]
Test on Differences (c)			
Unstratified p-value			0.3945

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.21.1: Effect Measures of Proportion of Subjects with Treatment Emergent Adverse Events in Surgical Phase - Renal and Urinary Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N=167)	RC + PLND (N=159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	10 (6.0%)	14 (8.8%)	
Number of patients without event	157 (94.0%)	145 (91.2%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			0.660 [0.284, 1.532]
Relative Risk (a)			
Unstratified RR, 95% CI			0.680 [0.311, 1.486]
Risk Difference (b)			
Unstratified RD, 95% CI			-0.028 [-0.085, 0.029]
Test on Differences (c)			
Unstratified p-value			0.3303

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.22.1: Effect Measures of Proportion of Subjects with Treatment Emergent Adverse Events in Surgical Phase - Respiratory, Thoracic and Mediastinal Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N=167)	RC + PLND (N=159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	7 (4.2%)	12 (7.5%)	
Number of patients without event	160 (95.8%)	147 (92.5%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			0.536 [0.205, 1.398]
Relative Risk (a)			
Unstratified RR, 95% CI			0.555 [0.224, 1.375]
Risk Difference (b)			
Unstratified RD, 95% CI			-0.034 [-0.085, 0.018]
Test on Differences (c)			
Unstratified p-value			0.1961

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.23.1: Effect Measures of Proportion of Subjects with Treatment Emergent Adverse Events in Surgical Phase - Vascular Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N=167)	RC + PLND (N=159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	8 (4.8%)	12 (7.5%)	
Number of patients without event	159 (95.2%)	147 (92.5%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			0.616 [0.245, 1.550]
Relative Risk (a)			
Unstratified RR, 95% CI			0.635 [0.266, 1.512]
Risk Difference (b)			
Unstratified RD, 95% CI			-0.028 [-0.080, 0.025]
Test on Differences (c)			
Unstratified p-value			0.2998

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 10% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.24.1: Effect Measures of Proportion of Subjects with Severe Treatment Emergent Adverse Events in Surgical Phase - Blood and Lymphatic System Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N=167)	RC + PLND (N=159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	7 (4.2%)	10 (6.3%)	
Number of patients without event	160 (95.8%)	149 (93.7%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			0.652 [0.242, 1.757]
Relative Risk (a)			
Unstratified RR, 95% CI			0.666 [0.260, 1.708]
Risk Difference (b)			
Unstratified RD, 95% CI			-0.021 [-0.069, 0.027]
Test on Differences (c)			
Unstratified p-value			0.3945

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.25.1: Effect Measures of Proportion of Subjects with Severe Treatment Emergent Adverse Events in Surgical Phase - Anaemia (PT)
SAF2 Analysis Set

	EV + Pembro (N=167)	RC + PLND (N=159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	7 (4.2%)	10 (6.3%)	
Number of patients without event	160 (95.8%)	149 (93.7%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			0.652 [0.242, 1.757]
Relative Risk (a)			
Unstratified RR, 95% CI			0.666 [0.260, 1.708]
Risk Difference (b)			
Unstratified RD, 95% CI			-0.021 [-0.069, 0.027]
Test on Differences (c)			
Unstratified p-value			0.3945

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.26.1: Effect Measures of Proportion of Subjects with Severe Treatment Emergent Adverse Events in Surgical Phase - Gastrointestinal Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N=167)	RC + PLND (N=159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	11 (6.6%)	16 (10.1%)	
Number of patients without event	156 (93.4%)	143 (89.9%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			0.630 [0.283, 1.403]
Relative Risk (a)			
Unstratified RR, 95% CI			0.655 [0.313, 1.367]
Risk Difference (b)			
Unstratified RD, 95% CI			-0.035 [-0.095, 0.025]
Test on Differences (c)			
Unstratified p-value			0.2550

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.27.1: Effect Measures of Proportion of Subjects with Severe Treatment Emergent Adverse Events in Surgical Phase - General Disorders and Administration Site Conditions (SOC)
SAF2 Analysis Set

	EV + Pembro (N=167)	**RC + PLND (N=159)**	**EV + Pembro vs. RC + PLND**
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	1 (0.6%)	10 (6.3%)	
Number of patients without event	166 (99.4%)	149 (93.7%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			0.090 [0.011, 0.710]
Relative Risk (a)			
Unstratified RR, 95% CI			0.095 [0.012, 0.735]
Risk Difference (b)			
Unstratified RD, 95% CI			-0.057 [-0.096, -0.017]
Test on Differences (c)			
Unstratified p-value			0.0048

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.27.2: Effect Measures of Proportion of Subjects with Severe Treatment Emergent Adverse Events in Surgical Phase by Subgroups - General Disorders and Administration Site Conditions (SOC)
SAF2 Analysis Set

Subgroup	EV + Pembro		RC + PLND		EV + Pembro vs. RC + PLND				
	N	n (%)	N	n (%)	Unstratified RR, 95% CI (a)	Unstratified OR, 95% CI (a)	Unstratified RD, 95% CI (b)	Difference p-value (c)	Interaction p-value (d)
Cisplatin Eligibility									
Ineligible	138	1 (0.7)	129	8 (6.2)	0.117 [0.015, 0.921]	0.110 [0.014, 0.895]	-0.055 [-0.099, -0.011]	0.0136	0.5323
Eligible but Declined	29	0 (0.0)	30	2 (6.7)	0.207 [0.010, 4.129]	0.193 [0.009, 4.203]	-0.067 [-0.156, 0.023]	0.2186	
Tumor Stage									
T2N0	31	1 (3.2)	27	2 (7.4)	0.435 [0.042, 4.541]	0.417 [0.036, 4.869]	-0.042 [-0.159, 0.075]	0.5898	NC
T3/T4aN0	129	0 (0.0)	125	8 (6.4)	0.057 [0.003, 0.977]	0.053 [0.003, 0.935]	-0.064 [-0.107, -0.021]	0.0035	
T1-4aN1	7	0 (0.0)	7	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC [NC, NC]	NC	
Geographical Regions									
US	21	0 (0.0)	23	1 (4.3)	0.364 [0.016, 8.468]	0.349 [0.013, 9.039]	-0.043 [-0.127, 0.040]	0.5138	NC
EU	76	1 (1.3)	69	6 (8.7)	0.151 [0.019, 1.226]	0.140 [0.016, 1.194]	-0.074 [-0.145, -0.003]	0.0403	
MOW	70	0 (0.0)	67	3 (4.5)	0.137 [0.007, 2.600]	0.131 [0.007, 2.579]	-0.045 [-0.094, 0.005]	0.0772	
Age Category									
< 65	29	1 (3.4)	28	1 (3.6)	0.966 [0.063, 14.697]	0.964 [0.057, 16.206]	-0.001 [-0.097, 0.094]	1.0000	0.0451
>= 65	138	0 (0.0)	131	9 (6.9)	0.050 [0.003, 0.850]	0.047 [0.003, 0.808]	-0.069 [-0.112, -0.025]	0.0017	
Sex									
Male	135	1 (0.7)	120	9 (7.5)	0.099 [0.013, 0.768]	0.092 [0.011, 0.738]	-0.068 [-0.117, -0.018]	0.0059	0.6983
Female	32	0 (0.0)	39	1 (2.6)	0.404 [0.017, 9.593]	0.395 [0.016, 10.027]	-0.026 [-0.075, 0.024]	0.5155	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; n=number of patients with events; NC=not calculated; OR=odds ratio; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; RD=risk difference; RR=relative risk; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences; (d) Type 3 likelihood ratio test p-value from binominal regression model with log-link including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.28.1: Effect Measures of Proportion of Subjects with Severe Treatment Emergent Adverse Events in Surgical Phase - Infections and Infestations (SOC)
SAF2 Analysis Set

	EV + Pembro (N=167)	RC + PLND (N=159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	25 (15.0%)	43 (27.0%)	
Number of patients without event	142 (85.0%)	116 (73.0%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			0.475 [0.274, 0.824]
Relative Risk (a)			
Unstratified RR, 95% CI			0.554 [0.356, 0.862]
Risk Difference (b)			
Unstratified RD, 95% CI			-0.121 [-0.208, -0.033]
Test on Differences (c)			
Unstratified p-value			0.0073

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.28.2: Effect Measures of Proportion of Subjects with Severe Treatment Emergent Adverse Events in Surgical Phase by Subgroups - Infections and Infestations (SOC)
SAF2 Analysis Set

Subgroup	EV + Pembro		RC + PLND		EV + Pembro vs. RC + PLND				
	N	n (%)	N	n (%)	Unstratified RR, 95% CI (a)	Unstratified OR, 95% CI (a)	Unstratified RD, 95% CI (b)	Difference p-value (c)	Interaction p-value (d)
Cisplatin Eligibility									
Ineligible	138	21 (15.2)	129	37 (28.7)	0.531 [0.329, 0.856]	0.446 [0.245, 0.814]	-0.135 [-0.233, -0.036]	0.0077	0.6846
Eligible but Declined	29	4 (13.8)	30	6 (20.0)	0.690 [0.217, 2.195]	0.640 [0.160, 2.553]	-0.062 [-0.252, 0.128]	0.6029	
Tumor Stage									
T2N0	31	5 (16.1)	27	6 (22.2)	0.726 [0.249, 2.113]	0.673 [0.180, 2.517]	-0.061 [-0.264, 0.142]	0.5549	0.7677
T3/T4aN0	129	19 (14.7)	125	34 (27.2)	0.541 [0.327, 0.897]	0.462 [0.247, 0.865]	-0.125 [-0.224, -0.026]	0.0145	
T1-4aN1	7	1 (14.3)	7	3 (42.9)	0.333 [0.045, 2.478]	0.222 [0.017, 2.970]	-0.286 [-0.735, 0.163]	0.3097	
Geographical Regions									
US	21	4 (19.0)	23	7 (30.4)	0.626 [0.213, 1.837]	0.538 [0.132, 2.193]	-0.114 [-0.366, 0.138]	0.5279	0.9099
EU	76	11 (14.5)	69	20 (29.0)	0.499 [0.258, 0.966]	0.415 [0.182, 0.945]	-0.145 [-0.278, -0.012]	0.0333	
MOW	70	10 (14.3)	67	16 (23.9)	0.598 [0.292, 1.224]	0.531 [0.222, 1.273]	-0.096 [-0.227, 0.035]	0.1522	
Age Category									
< 65	29	7 (24.1)	28	6 (21.4)	1.126 [0.432, 2.938]	1.167 [0.338, 4.033]	0.027 [-0.191, 0.245]	0.8075	0.1083
>= 65	138	18 (13.0)	131	37 (28.2)	0.462 [0.277, 0.769]	0.381 [0.204, 0.712]	-0.152 [-0.247, -0.057]	0.0020	
Sex									
Male	135	20 (14.8)	120	32 (26.7)	0.556 [0.336, 0.917]	0.478 [0.256, 0.892]	-0.119 [-0.218, -0.019]	0.0190	0.9959
Female	32	5 (15.6)	39	11 (28.2)	0.554 [0.215, 1.430]	0.471 [0.145, 1.537]	-0.126 [-0.315, 0.063]	0.2068	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; n=number of patients with events; NC=not calculated; OR=odds ratio; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; RD=risk difference; RR=relative risk; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences; (d) Type 3 likelihood ratio test p-value from binominal regression model with log-link including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.29.1: Effect Measures of Proportion of Subjects with Severe Treatment Emergent Adverse Events in Surgical Phase - Urinary Tract Infection (PT)
SAF2 Analysis Set

	EV + Pembro (N=167)	RC + PLND (N=159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	8 (4.8%)	17 (10.7%)	
Number of patients without event	159 (95.2%)	142 (89.3%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			0.420 [0.176, 1.003]
Relative Risk (a)			
Unstratified RR, 95% CI			0.448 [0.199, 1.009]
Risk Difference (b)			
Unstratified RD, 95% CI			-0.059 [-0.117, -0.001]
Test on Differences (c)			
Unstratified p-value			0.0453

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.29.2: Effect Measures of Proportion of Subjects with Severe Treatment Emergent Adverse Events in Surgical Phase by Subgroups - Urinary Tract Infection (PT)
SAF2 Analysis Set

Subgroup	EV + Pembro		RC + PLND		EV + Pembro vs. RC + PLND				
	N	n (%)	N	n (%)	Unstratified RR, 95% CI (a)	Unstratified OR, 95% CI (a)	Unstratified RD, 95% CI (b)	Difference p-value (c)	Interaction p-value (d)
Cisplatin Eligibility									
Ineligible	138	8 (5.8)	129	14 (10.9)	0.534 [0.232, 1.231]	0.505 [0.205, 1.249]	-0.051 [-0.117, 0.016]	0.1333	0.1226
Eligible but Declined	29	0 (0.0)	30	3 (10.0)	0.148 [0.008, 2.738]	0.133 [0.007, 2.697]	-0.100 [-0.207, 0.007]	0.1000	
Tumor Stage									
T2N0	31	2 (6.5)	27	0 (0.0)	4.375 [0.219, 87.323]	4.661 [0.214, 101.47]	0.065 [-0.022, 0.151]	0.2202	NC
T3/T4aN0	129	6 (4.7)	125	16 (12.8)	0.363 [0.147, 0.899]	0.332 [0.126, 0.879]	-0.081 [-0.150, -0.013]	0.0210	
T1-4aN1	7	0 (0.0)	7	1 (14.3)	0.333 [0.016, 7.017]	0.289 [0.010, 8.388]	-0.143 [-0.402, 0.116]	0.5199	
Geographical Regions									
US	21	1 (4.8)	23	1 (4.3)	1.095 [0.073, 16.427]	1.100 [0.064, 18.774]	0.004 [-0.119, 0.128]	0.9999	0.7703
EU	76	4 (5.3)	69	8 (11.6)	0.454 [0.143, 1.441]	0.424 [0.122, 1.475]	-0.063 [-0.154, 0.027]	0.1819	
MOW	70	3 (4.3)	67	8 (11.9)	0.359 [0.099, 1.296]	0.330 [0.084, 1.302]	-0.077 [-0.168, 0.014]	0.1095	
Age Category									
< 65	29	3 (10.3)	28	3 (10.7)	0.966 [0.213, 4.387]	0.962 [0.177, 5.221]	-0.004 [-0.163, 0.156]	1.0000	0.2591
>= 65	138	5 (3.6)	131	14 (10.7)	0.339 [0.126, 0.915]	0.314 [0.110, 0.899]	-0.071 [-0.132, -0.009]	0.0238	
Sex									
Male	135	7 (5.2)	120	12 (10.0)	0.519 [0.211, 1.274]	0.492 [0.187, 1.294]	-0.048 [-0.114, 0.017]	0.1439	0.4911
Female	32	1 (3.1)	39	5 (12.8)	0.244 [0.030, 1.982]	0.219 [0.024, 1.983]	-0.097 [-0.218, 0.024]	0.1787	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; n=number of patients with events; NC=not calculated; OR=odds ratio; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; RD=risk difference; RR=relative risk; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences; (d) Type 3 likelihood ratio test p-value from binominal regression model with log-link including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.30.1: Effect Measures of Proportion of Subjects with Severe Treatment Emergent Adverse Events in Surgical Phase - Injury, Poisoning and Procedural Complications (SOC)
SAF2 Analysis Set

	EV + Pembro (N=167)	RC + PLND (N=159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	9 (5.4%)	12 (7.5%)	
Number of patients without event	158 (94.6%)	147 (92.5%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			0.698 [0.286, 1.704]
Relative Risk (a)			
Unstratified RR, 95% CI			0.714 [0.309, 1.648]
Risk Difference (b)			
Unstratified RD, 95% CI			-0.022 [-0.075, 0.032]
Test on Differences (c)			
Unstratified p-value			0.4276

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.31.1: Effect Measures of Proportion of Subjects with Severe Treatment Emergent Adverse Events in Surgical Phase - Renal and Urinary Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N=167)	RC + PLND (N=159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	4 (2.4%)	8 (5.0%)	
Number of patients without event	163 (97.6%)	151 (95.0%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			0.463 [0.137, 1.570]
Relative Risk (a)			
Unstratified RR, 95% CI			0.476 [0.146, 1.550]
Risk Difference (b)			
Unstratified RD, 95% CI			-0.026 [-0.067, 0.015]
Test on Differences (c)			
Unstratified p-value			0.2467

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.32.1: Effect Measures of Proportion of Subjects with Serious Treatment Emergent Adverse Events in Surgical Phase - Gastrointestinal Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N=167)	**RC + PLND (N=159)**	**EV + Pembro vs. RC + PLND**
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	8 (4.8%)	12 (7.5%)	
Number of patients without event	159 (95.2%)	147 (92.5%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			0.616 [0.245, 1.550]
Relative Risk (a)			
Unstratified RR, 95% CI			0.635 [0.266, 1.512]
Risk Difference (b)			
Unstratified RD, 95% CI			-0.028 [-0.080, 0.025]
Test on Differences (c)			
Unstratified p-value			0.2998

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.33.1: Effect Measures of Proportion of Subjects with Serious Treatment Emergent Adverse Events in Surgical Phase - General Disorders and Administration Site Conditions (SOC)
SAF2 Analysis Set

	EV + Pembro (N=167)	RC + PLND (N=159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	1 (0.6%)	8 (5.0%)	
Number of patients without event	166 (99.4%)	151 (95.0%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			0.114 [0.014, 0.920]
Relative Risk (a)			
Unstratified RR, 95% CI			0.119 [0.015, 0.941]
Risk Difference (b)			
Unstratified RD, 95% CI			-0.044 [-0.080, -0.008]
Test on Differences (c)			
Unstratified p-value			0.0149

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.33.2: Effect Measures of Proportion of Subjects with Serious Treatment Emergent Adverse Events in Surgical Phase by Subgroups - General Disorders and Administration Site Conditions (SOC)
SAF2 Analysis Set

Subgroup	EV + Pembro		RC + PLND		EV + Pembro vs. RC + PLND				
	N	n (%)	N	n (%)	Unstratified RR, 95% CI (a)	Unstratified OR, 95% CI (a)	Unstratified RD, 95% CI (b)	Difference p-value (c)	Interaction p-value (d)
Cisplatin Eligibility									
Ineligible	138	1 (0.7)	129	6 (4.7)	0.156 [0.019, 1.277]	0.150 [0.018, 1.260]	-0.039 [-0.078, 0.000]	0.0495	0.4806
Eligible but Declined	29	0 (0.0)	30	2 (6.7)	0.207 [0.010, 4.129]	0.193 [0.009, 4.203]	-0.067 [-0.156, 0.023]	0.2186	
Tumor Stage									
T2N0	31	1 (3.2)	27	1 (3.7)	0.871 [0.057, 13.266]	0.867 [0.052, 14.556]	-0.005 [-0.099, 0.090]	0.9934	NC
T3/T4aN0	129	0 (0.0)	125	7 (5.6)	0.065 [0.004, 1.120]	0.061 [0.003, 1.080]	-0.056 [-0.096, -0.016]	0.0069	
T1-4aN1	7	0 (0.0)	7	0 (0.0)	NC [NC, NC]	NC [NC, NC]	NC [NC, NC]	NC	
Geographical Regions									
US	21	0 (0.0)	23	1 (4.3)	0.364 [0.016, 8.468]	0.349 [0.013, 9.039]	-0.043 [-0.127, 0.040]	0.5138	NC
EU	76	1 (1.3)	69	5 (7.2)	0.182 [0.022, 1.516]	0.171 [0.019, 1.499]	-0.059 [-0.126, 0.007]	0.0887	
MOW	70	0 (0.0)	67	2 (3.0)	0.192 [0.009, 3.918]	0.186 [0.009, 3.943]	-0.030 [-0.071, 0.011]	0.1537	
Age Category									
< 65	29	1 (3.4)	28	1 (3.6)	0.966 [0.063, 14.697]	0.964 [0.057, 16.206]	-0.001 [-0.097, 0.094]	1.0000	0.0583
>= 65	138	0 (0.0)	131	7 (5.3)	0.063 [0.004, 1.098]	0.060 [0.003, 1.060]	-0.053 [-0.092, -0.015]	0.0061	
Sex									
Male	135	1 (0.7)	120	7 (5.8)	0.127 [0.016, 1.017]	0.120 [0.015, 0.994]	-0.051 [-0.095, -0.007]	0.0207	0.6635
Female	32	0 (0.0)	39	1 (2.6)	0.404 [0.017, 9.593]	0.395 [0.016, 10.027]	-0.026 [-0.075, 0.024]	0.5155	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; n=number of patients with events; NC=not calculated; OR=odds ratio; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; RD=risk difference; RR=relative risk; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences; (d) Type 3 likelihood ratio test p-value from binominal regression model with log-link including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.34.1: Effect Measures of Proportion of Subjects with Serious Treatment Emergent Adverse Events in Surgical Phase - Infections and Infestations (SOC)
SAF2 Analysis Set

	EV + Pembro (N=167)	RC + PLND (N=159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	21 (12.6%)	37 (23.3%)	
Number of patients without event	146 (87.4%)	122 (76.7%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			0.474 [0.264, 0.853]
Relative Risk (a)			
Unstratified RR, 95% CI			0.540 [0.331, 0.882]
Risk Difference (b)			
Unstratified RD, 95% CI			-0.107 [-0.190, -0.024]
Test on Differences (c)			
Unstratified p-value			0.0116

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.34.2: Effect Measures of Proportion of Subjects with Serious Treatment Emergent Adverse Events in Surgical Phase by Subgroups - Infections and Infestations (SOC)
SAF2 Analysis Set

Subgroup	EV + Pembro		RC + PLND		EV + Pembro vs. RC + PLND				
	N	n (%)	N	n (%)	Unstratified RR, 95% CI (a)	Unstratified OR, 95% CI (a)	Unstratified RD, 95% CI (b)	Difference p-value (c)	Interaction p-value (d)
Cisplatin Eligibility									
Ineligible	138	18 (13.0)	129	33 (25.6)	0.510 [0.303, 0.859]	0.436 [0.231, 0.823]	-0.125 [-0.219, -0.031]	0.0092	0.5884
Eligible but Declined	29	3 (10.3)	30	4 (13.3)	0.776 [0.190, 3.169]	0.750 [0.153, 3.687]	-0.030 [-0.194, 0.135]	0.8023	
Tumor Stage									
T2N0	31	5 (16.1)	27	6 (22.2)	0.726 [0.249, 2.113]	0.673 [0.180, 2.517]	-0.061 [-0.264, 0.142]	0.5549	0.7569
T3/T4aN0	129	15 (11.6)	125	28 (22.4)	0.519 [0.292, 0.924]	0.456 [0.230, 0.903]	-0.108 [-0.199, -0.016]	0.0221	
T1-4aN1	7	1 (14.3)	7	3 (42.9)	0.333 [0.045, 2.478]	0.222 [0.017, 2.970]	-0.286 [-0.735, 0.163]	0.3097	
Geographical Regions									
US	21	2 (9.5)	23	6 (26.1)	0.365 [0.083, 1.615]	0.298 [0.053, 1.680]	-0.166 [-0.385, 0.053]	0.1748	0.7994
EU	76	11 (14.5)	69	19 (27.5)	0.526 [0.270, 1.024]	0.445 [0.194, 1.020]	-0.131 [-0.262, 0.001]	0.0525	
MOW	70	8 (11.4)	67	12 (17.9)	0.638 [0.278, 1.463]	0.591 [0.225, 1.553]	-0.065 [-0.183, 0.053]	0.2828	
Age Category									
< 65	29	5 (17.2)	28	6 (21.4)	0.805 [0.277, 2.339]	0.764 [0.204, 2.860]	-0.042 [-0.247, 0.163]	0.6888	0.4235
>= 65	138	16 (11.6)	131	31 (23.7)	0.490 [0.282, 0.853]	0.423 [0.219, 0.817]	-0.121 [-0.211, -0.030]	0.0092	
Sex									
Male	135	17 (12.6)	120	27 (22.5)	0.560 [0.321, 0.975]	0.496 [0.255, 0.965]	-0.099 [-0.192, -0.006]	0.0366	0.8198
Female	32	4 (12.5)	39	10 (25.6)	0.488 [0.169, 1.409]	0.414 [0.116, 1.476]	-0.131 [-0.310, 0.047]	0.1882	

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; n=number of patients with events; NC=not calculated; OR=odds ratio; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; RD=risk difference; RR=relative risk; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences; (d) Type 3 likelihood ratio test p-value from binominal regression model with log-link including treatment, subgroup, and treatment x subgroup interaction.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.35.1: Effect Measures of Proportion of Subjects with Serious Treatment Emergent Adverse Events in Surgical Phase - Urinary Tract Infection (PT)
SAF2 Analysis Set

	EV + Pembro (N=167)	**RC + PLND (N=159)**	**EV + Pembro vs. RC + PLND**
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	7 (4.2%)	15 (9.4%)	
Number of patients without event	160 (95.8%)	144 (90.6%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			0.420 [0.167, 1.059]
Relative Risk (a)			
Unstratified RR, 95% CI			0.444 [0.186, 1.061]
Risk Difference (b)			
Unstratified RD, 95% CI			-0.052 [-0.107, 0.002]
Test on Differences (c)			
Unstratified p-value			0.0593

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.36.1: Effect Measures of Proportion of Subjects with Serious Treatment Emergent Adverse Events in Surgical Phase - Injury, Poisoning and Procedural Complications (SOC)
SAF2 Analysis Set

	EV + Pembro (N=167)	**RC + PLND (N=159)**	**EV + Pembro vs. RC + PLND**
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	10 (6.0%)	7 (4.4%)	
Number of patients without event	157 (94.0%)	152 (95.6%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			1.383 [0.513, 3.727]
Relative Risk (a)			
Unstratified RR, 95% CI			1.360 [0.531, 3.486]
Risk Difference (b)			
Unstratified RD, 95% CI			0.016 [-0.032, 0.064]
Test on Differences (c)			
Unstratified p-value			0.5198

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25

Table 303.1.2002.37.1: Effect Measures of Proportion of Subjects with Serious Treatment Emergent Adverse Events in Surgical Phase - Renal and Urinary Disorders (SOC)
SAF2 Analysis Set

	EV + Pembro (N=167)	RC + PLND (N=159)	EV + Pembro vs. RC + PLND
Number of patients at risk	167 (100.0%)	159 (100.0%)	
Number of patients with events	6 (3.6%)	8 (5.0%)	
Number of patients without event	161 (96.4%)	151 (95.0%)	
Odds Ratio (a)			
Unstratified OR, 95% CI			0.703 [0.239, 2.075]
Relative Risk (a)			
Unstratified RR, 95% CI			0.714 [0.253, 2.012]
Risk Difference (b)			
Unstratified RD, 95% CI			-0.014 [-0.059, 0.030]
Test on Differences (c)			
Unstratified p-value			0.5219

Abbreviations: CI=confidence interval; EV=enfortumab vedotin; N=number of patients; NC=not calculated; Pembro=pembrolizumab; PLND=pelvic lymph node dissection; PT=preferred term; RC=radical cystectomy; SOC=system organ class.
(a) Estimated using unstratified Cochran–Mantel–Haenszel method with zero cell correction; (b) Absolute risk difference of EV + Pembro and RC + PLND with 95% confidence interval based on the Wald method;
(c) Two-sided p-value based on Chi-square test or Barnard's exact test (if any cell count is <5) for treatment differences.
Note: The SAF2 analysis set includes all patients that are randomized into arms B and C in stage 2 who received any amount of study treatment.
SOCs and PTs are reported only if events are either 1) occurring in at least 5% of patients in at least one treatment group; OR 2) occurring in at least 10 patients in at least one treatment group and at least 1% of patients in at least one treatment group.
ASTELLAS Data Cutoff Date (EV-303): 06JUN25