Dossier zur Nutzenbewertung gemäß § 35a SGB V

Enfortumab Vedotin (PADCEV™)

Astellas Pharma GmbH

Anhang 4-G1

1. Datenschnitt vom 15.07.2020
zur Studienpopulation

Stand: 24.05.2022

Inhaltsverzeichnis

Seite

1 Mortalität

1.1 Subgruppenanalysen zum Gesamtüberleben (OS)

Astellas: 7465-CL-0301
Table OS.KM.S1.FAS: Time to Overall Survival (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	49 (45.4)	66 (59.5)
	Median Survival Est. (95% CI)	11.04 (9.99, 15.34)	8.31 (7.03, 10.68)
	Hazard Ratio (95% CI)		0.680 (0.470, 0.985)
	Treatment P-value [a]		0.04061
	Interaction P-value [b]		0.70606
6 Months	Patients at Risk, Survival Est. (95% CI)	83, 0.80 (0.71, 0.87)	69, 0.66 (0.56, 0.74)
12 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.47 (0.35, 0.58)	17, 0.33 (0.23, 0.43)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.24 (0.09, 0.43)	2, 0.22 (0.07, 0.42)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table OS.KM.S1.FAS: Time to Overall Survival (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	85 (44.0)	101 (51.5)
	Median Survival Est. (95% CI)	14.32 (10.05, 17.15)	9.46 (8.44, 13.70)
	Hazard Ratio (95% CI)		0.745 (0.558, 0.994)
	Treatment P-value [a]		0.04580
	Interaction P-value [b]		0.70606
6 Months	Patients at Risk, Survival Est. (95% CI)	139, 0.77 (0.70, 0.82)	129, 0.72 (0.65, 0.77)
12 Months	Patients at Risk, Survival Est. (95% CI)	46, 0.54 (0.45, 0.62)	34, 0.43 (0.35, 0.52)
18 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.31 (0.18, 0.45)	4, 0.23 (0.13, 0.35)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
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Table OS.KM.S2.FAS: Time to Overall Survival (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	109 (43.8)	128 (53.6)
	Median Survival Est. (95% CI)	14.13 (10.58, 17.15)	9.17 (8.05, 10.91)
	Hazard Ratio (95% CI)		0.686 (0.531, 0.885)
	Treatment P-value [a]		0.00410
	Interaction P-value [b]		0.35828
6 Months	Patients at Risk, Survival Est. (95% CI)	188, 0.79 (0.73, 0.83)	151, 0.68 (0.61, 0.73)
12 Months	Patients at Risk, Survival Est. (95% CI)	54, 0.52 (0.45, 0.59)	37, 0.39 (0.32, 0.47)
18 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.30 (0.17, 0.43)	4, 0.22 (0.12, 0.35)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Table OS.KM.S2.FAS: Time to Overall Survival (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	25 (48.1)	39 (57.4)
	Median Survival Est. (95% CI)	11.63 (8.44, 15.21)	8.94 (7.52, 13.60)
	Hazard Ratio (95% CI)		0.893 (0.540, 1.476)
	Treatment P-value [a]		0.71280
	Interaction P-value [b]		0.35828
6 Months	Patients at Risk, Survival Est. (95% CI)	34, 0.74 (0.59, 0.84)	47, 0.76 (0.63, 0.84)
12 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.47 (0.30, 0.63)	14, 0.39 (0.26, 0.52)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.13 (0.01, 0.41)	2, 0.22 (0.10, 0.38)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Table OS.KM.S3.FAS: Time to Overall Survival (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	101 (42.4)	132 (56.9)
	Median Survival Est. (95% CI)	14.32 (10.58, 17.25)	8.94 (8.05, 10.32)
	Hazard Ratio (95% CI)		0.614 (0.473, 0.796)
	Treatment P-value [a]		0.00016
	Interaction P-value [b]		0.01342
6 Months	Patients at Risk, Survival Est. (95% CI)	178, 0.80 (0.74, 0.84)	148, 0.68 (0.62, 0.74)
12 Months	Patients at Risk, Survival Est. (95% CI)	54, 0.54 (0.46, 0.61)	35, 0.37 (0.29, 0.44)
18 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.32 (0.20, 0.45)	2, 0.17 (0.07, 0.30)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Table OS.KM.S3.FAS: Time to Overall Survival (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	33 (52.4)	35 (46.7)
	Median Survival Est. (95% CI)	11.04 (7.95, 15.11)	10.68 (7.36, NC)
	Hazard Ratio (95% CI)		1.222 (0.757, 1.973)
	Treatment P-value [a]		0.51787
	Interaction P-value [b]		0.01342
6 Months	Patients at Risk, Survival Est. (95% CI)	44, 0.71 (0.59, 0.81)	50, 0.73 (0.62, 0.82)
12 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.41 (0.26, 0.56)	16, 0.46 (0.32, 0.58)
18 Months	Patients at Risk, Survival Est. (95% CI)	0	4, 0.38 (0.21, 0.55)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Table OS.KM.S4.FAS: Time to Overall Survival (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	57 (45.2)	72 (55.8)
	Median Survival Est. (95% CI)	12.88 (8.44, NC)	9.17 (7.10, 13.70)
	Hazard Ratio (95% CI)		0.728 (0.514, 1.032)
	Treatment P-value [a]		0.11773
	Interaction P-value [b]		0.69206
6 Months	Patients at Risk, Survival Est. (95% CI)	89, 0.74 (0.66, 0.81)	78, 0.65 (0.56, 0.73)
12 Months	Patients at Risk, Survival Est. (95% CI)	24, 0.52 (0.41, 0.61)	21, 0.43 (0.33, 0.52)
18 Months	Patients at Risk, Survival Est. (95% CI)	0	3, 0.19 (0.07, 0.35)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Table OS.KM.S4.FAS: Time to Overall Survival (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	25 (58.1)	25 (56.8)
	Median Survival Est. (95% CI)	10.45 (7.52, 20.27)	8.94 (6.05, 16.72)
	Hazard Ratio (95% CI)		0.874 (0.502, 1.523)
	Treatment P-value [a]		0.65734
	Interaction P-value [b]		0.69206
6 Months	Patients at Risk, Survival Est. (95% CI)	30, 0.75 (0.59, 0.86)	27, 0.68 (0.51, 0.80)
12 Months	Patients at Risk, Survival Est. (95% CI)	14, 0.45 (0.29, 0.59)	13, 0.44 (0.29, 0.59)
18 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.34 (0.17, 0.52)	1, 0.25 (0.09, 0.45)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

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Table OS.KM.S4.FAS: Time to Overall Survival (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	52 (39.4)	70 (52.2)
	Median Survival Est. (95% CI)	14.85 (10.84, 15.21)	8.97 (7.85, 10.87)
	Hazard Ratio (95% CI)		0.656 (0.458, 0.939)
	Treatment P-value [a]		0.01506
	Interaction P-value [b]		0.69206
6 Months	Patients at Risk, Survival Est. (95% CI)	103, 0.82 (0.74, 0.88)	93, 0.74 (0.66, 0.81)
12 Months	Patients at Risk, Survival Est. (95% CI)	25, 0.54 (0.43, 0.64)	17, 0.33 (0.23, 0.43)
18 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.25 (0.11, 0.42)	2, 0.30 (0.19, 0.41)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Table OS.KM.S5.FAS: Time to Overall Survival (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	40 (33.3)	46 (37.1)
	Median Survival Est. (95% CI)	16.30 (12.88, NC)	15.44 (10.05, NC)
	Hazard Ratio (95% CI)		0.829 (0.543, 1.267)
	Treatment P-value [a]		0.33248
	Interaction P-value [b]		0.36493
6 Months	Patients at Risk, Survival Est. (95% CI)	102, 0.87 (0.80, 0.92)	103, 0.89 (0.82, 0.94)
12 Months	Patients at Risk, Survival Est. (95% CI)	31, 0.63 (0.52, 0.73)	23, 0.52 (0.40, 0.63)
18 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.38 (0.19, 0.56)	4, 0.41 (0.23, 0.57)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Table OS.KM.S5.FAS: Time to Overall Survival (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	94 (51.9)	121 (66.1)
	Median Survival Est. (95% CI)	10.45 (8.28, 14.13)	7.06 (5.85, 8.31)
	Hazard Ratio (95% CI)		0.657 (0.502, 0.861)
	Treatment P-value [a]		0.00302
	Interaction P-value [b]		0.36493
6 Months	Patients at Risk, Survival Est. (95% CI)	120, 0.72 (0.64, 0.78)	95, 0.56 (0.48, 0.63)
12 Months	Patients at Risk, Survival Est. (95% CI)	32, 0.44 (0.35, 0.52)	28, 0.31 (0.23, 0.38)
18 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.23 (0.11, 0.38)	2, 0.12 (0.04, 0.23)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Table OS.KM.S6.FAS: Time to Overall Survival (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	53 (57.0)	63 (66.3)
	Median Survival Est. (95% CI)	9.63 (6.80, 11.63)	5.95 (4.93, 7.10)
	Hazard Ratio (95% CI)		0.631 (0.437, 0.911)
	Treatment P-value [a]		0.02724
	Interaction P-value [b]		0.52576
6 Months	Patients at Risk, Survival Est. (95% CI)	53, 0.63 (0.52, 0.72)	42, 0.50 (0.39, 0.59)
12 Months	Patients at Risk, Survival Est. (95% CI)	14, 0.37 (0.26, 0.49)	7, 0.24 (0.14, 0.36)
18 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.20 (0.06, 0.40)	1, 0.13 (0.03, 0.29)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

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Table OS.KM.S6.FAS: Time to Overall Survival (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	81 (38.9)	104 (49.1)
	Median Survival Est. (95% CI)	15.18 (11.63, 17.87)	10.74 (9.17, 14.06)
	Hazard Ratio (95% CI)		0.734 (0.549, 0.982)
	Treatment P-value [a]		0.03639
	Interaction P-value [b]		0.52576
6 Months	Patients at Risk, Survival Est. (95% CI)	169, 0.84 (0.79, 0.89)	156, 0.78 (0.72, 0.83)
12 Months	Patients at Risk, Survival Est. (95% CI)	49, 0.58 (0.49, 0.65)	44, 0.46 (0.38, 0.53)
18 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.32 (0.17, 0.47)	5, 0.27 (0.16, 0.39)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Analysis Plan: 15FEB2021 Confidential

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Table OS.KM.S7.FAS: Time to Overall Survival (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	63 (44.7)	59 (52.7)
	Median Survival Est. (95% CI)	14.32 (10.15, 17.25)	9.20 (7.62, 13.70)
	Hazard Ratio (95% CI)		0.706 (0.495, 1.008)
	Treatment P-value [a]		0.05373
	Interaction P-value [b]		0.97726
6 Months	Patients at Risk, Survival Est. (95% CI)	105, 0.79 (0.71, 0.85)	69, 0.66 (0.56, 0.74)
12 Months	Patients at Risk, Survival Est. (95% CI)	35, 0.51 (0.41, 0.60)	18, 0.41 (0.30, 0.52)
18 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.25 (0.10, 0.44)	2, 0.24 (0.12, 0.38)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table OS.KM.S7.FAS: Time to Overall Survival (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	41 (47.1)	67 (57.3)
	Median Survival Est. (95% CI)	12.62 (9.63, 17.15)	8.44 (7.52, 10.68)
	Hazard Ratio (95% CI)		0.713 (0.483, 1.053)
	Treatment P-value [a]		0.07904
	Interaction P-value [b]		0.97726
6 Months	Patients at Risk, Survival Est. (95% CI)	67, 0.79 (0.69, 0.86)	81, 0.73 (0.64, 0.80)
12 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.50 (0.38, 0.62)	21, 0.37 (0.27, 0.46)
18 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.30 (0.15, 0.47)	3, 0.29 (0.17, 0.42)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table OS.KM.S7.FAS: Time to Overall Survival (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	30 (41.1)	41 (52.6)
	Median Survival Est. (95% CI)	14.13 (8.08, NC)	9.46 (7.36, 13.70)
	Hazard Ratio (95% CI)		0.752 (0.469, 1.204)
	Treatment P-value [a]		0.27837
	Interaction P-value [b]		0.97726
6 Months	Patients at Risk, Survival Est. (95% CI)	50, 0.75 (0.63, 0.83)	48, 0.69 (0.57, 0.78)
12 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.57 (0.43, 0.68)	12, 0.41 (0.27, 0.54)
18 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.12 (0.01, 0.37)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table OS.KM.S8.FAS: Time to Overall Survival (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	44 (44.9)	52 (48.6)
	Median Survival Est. (95% CI)	12.62 (10.05, 15.34)	10.91 (8.05, 14.06)
	Hazard Ratio (95% CI)		0.839 (0.561, 1.253)
	Treatment P-value [a]		0.42338
	Interaction P-value [b]		0.34983
6 Months	Patients at Risk, Survival Est. (95% CI)	73, 0.78 (0.68, 0.85)	75, 0.75 (0.65, 0.82)
12 Months	Patients at Risk, Survival Est. (95% CI)	23, 0.51 (0.38, 0.62)	21, 0.46 (0.34, 0.57)
18 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.30 (0.15, 0.46)	1, 0.29 (0.15, 0.44)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table OS.KM.S8.FAS: Time to Overall Survival (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	90 (44.3)	115 (57.5)
	Median Survival Est. (95% CI)	14.13 (9.79, 17.15)	8.51 (7.62, 10.15)
	Hazard Ratio (95% CI)		0.665 (0.504, 0.876)
	Treatment P-value [a]		0.00374
	Interaction P-value [b]		0.34983
6 Months	Patients at Risk, Survival Est. (95% CI)	149, 0.78 (0.72, 0.83)	123, 0.67 (0.59, 0.73)
12 Months	Patients at Risk, Survival Est. (95% CI)	40, 0.52 (0.44, 0.60)	30, 0.36 (0.28, 0.44)
18 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.29 (0.16, 0.44)	5, 0.21 (0.11, 0.33)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table OS.KM.S9.FAS: Time to Overall Survival (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	115 (43.9)	147 (54.4)
	Median Survival Est. (95% CI)	14.13 (10.84, 15.34)	8.94 (8.05, 10.87)
	Hazard Ratio (95% CI)		0.691 (0.541, 0.882)
	Treatment P-value [a]		0.00297
	Interaction P-value [b]		0.37635
6 Months	Patients at Risk, Survival Est. (95% CI)	193, 0.78 (0.72, 0.82)	173, 0.69 (0.63, 0.75)
12 Months	Patients at Risk, Survival Est. (95% CI)	57, 0.53 (0.45, 0.59)	45, 0.40 (0.33, 0.47)
18 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.29 (0.17, 0.42)	5, 0.21 (0.12, 0.31)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table OS.KM.S9.FAS: Time to Overall Survival (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	19 (48.7)	20 (54.1)
	Median Survival Est. (95% CI)	9.10 (7.49, NC)	10.55 (6.67, NC)
	Hazard Ratio (95% CI)		0.937 (0.500, 1.757)
	Treatment P-value [a]		0.68399
	Interaction P-value [b]		0.37635
6 Months	Patients at Risk, Survival Est. (95% CI)	29, 0.79 (0.63, 0.89)	25, 0.70 (0.53, 0.82)
12 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.46 (0.27, 0.62)	6, 0.35 (0.18, 0.53)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.23 (0.02, 0.57)	1, 0.35 (0.18, 0.53)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table OS.KM.S10.FAS: Time to Overall Survival (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	18 (29.5)	23 (46.0)
	Median Survival Est. (95% CI)	NC (10.84, NC)	11.56 (8.05, NC)
	Hazard Ratio (95% CI)		0.626 (0.338, 1.160)
	Treatment P-value [a]		0.14264
	Interaction P-value [b]		0.57697
6 Months	Patients at Risk, Survival Est. (95% CI)	49, 0.85 (0.73, 0.92)	39, 0.80 (0.65, 0.88)
12 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.63 (0.45, 0.76)	9, 0.46 (0.29, 0.62)
18 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.46 (0.29, 0.62)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table OS.KM.S10.FAS: Time to Overall Survival (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	100 (48.3)	120 (55.8)
	Median Survival Est. (95% CI)	11.63 (9.99, 15.18)	9.17 (7.95, 10.74)
	Hazard Ratio (95% CI)		0.758 (0.581, 0.989)
	Treatment P-value [a]		0.03981
	Interaction P-value [b]		0.57697
6 Months	Patients at Risk, Survival Est. (95% CI)	150, 0.77 (0.70, 0.82)	134, 0.68 (0.61, 0.74)
12 Months	Patients at Risk, Survival Est. (95% CI)	42, 0.48 (0.40, 0.56)	37, 0.38 (0.30, 0.45)
18 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.25 (0.14, 0.38)	5, 0.20 (0.12, 0.30)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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2 Morbidität

2.1 Subgruppenanalysen zum Progressionsfreien Überleben 1 (PFS1)

2.1.1 Primäranalyse

Astellas: 7465-CL-0301
Table PFS1.KM.S1.FAS: Time to Progression-Free Survival on Study Therapy (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	75 (69.4)	80 (72.1)
	Median Survival Est. (95% CI)	5.45 (3.94, 6.34)	3.55 (2.37, 3.84)
	Hazard Ratio (95% CI)		0.697 (0.508, 0.955)
	Treatment P-value [a]		0.02888
	Interaction P-value [b]		0.55074
6 Months	Patients at Risk, Survival Est. (95% CI)	37, 0.43 (0.33, 0.53)	23, 0.27 (0.19, 0.37)
12 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.19 (0.11, 0.28)	1, 0.05 (0.01, 0.17)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.16 (0.08, 0.26)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table PFS1.KM.S1.FAS: Time to Progression-Free Survival on Study Therapy (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	126 (65.3)	151 (77.0)
	Median Survival Est. (95% CI)	5.65 (5.22, 7.16)	3.78 (3.52, 4.90)
	Hazard Ratio (95% CI)		0.618 (0.487, 0.784)
	Treatment P-value [a]		0.00005
	Interaction P-value [b]		0.55074
6 Months	Patients at Risk, Survival Est. (95% CI)	65, 0.45 (0.37, 0.52)	39, 0.29 (0.22, 0.36)
12 Months	Patients at Risk, Survival Est. (95% CI)	16, 0.24 (0.17, 0.31)	7, 0.09 (0.05, 0.15)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.16 (0.09, 0.25)	1, 0.03 (0.00, 0.10)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table PFS1.KM.S2.FAS: Time to Progression-Free Survival on Study Therapy (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	166 (66.7)	180 (75.3)
	Median Survival Est. (95% CI)	5.62 (5.32, 6.34)	3.65 (3.32, 3.84)
	Hazard Ratio (95% CI)		0.602 (0.486, 0.744)
	Treatment P-value [a]		<.00001
	Interaction P-value [b]		0.11908
6 Months	Patients at Risk, Survival Est. (95% CI)	89, 0.45 (0.38, 0.51)	48, 0.28 (0.22, 0.34)
12 Months	Patients at Risk, Survival Est. (95% CI)	22, 0.23 (0.17, 0.30)	5, 0.07 (0.03, 0.13)
18 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.19 (0.13, 0.26)	1, 0.03 (0.00, 0.12)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table PFS1.KM.S2.FAS: Time to Progression-Free Survival on Study Therapy (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	35 (67.3)	51 (75.0)
	Median Survival Est. (95% CI)	5.42 (3.71, 7.20)	3.84 (3.52, 5.62)
	Hazard Ratio (95% CI)		0.881 (0.573, 1.355)
	Treatment P-value [a]		0.59896
	Interaction P-value [b]		0.11908
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.40 (0.25, 0.54)	14, 0.31 (0.19, 0.43)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.13 (0.04, 0.27)	3, 0.12 (0.05, 0.24)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table PFS1.KM.S3.FAS: Time to Progression-Free Survival on Study Therapy (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	153 (64.3)	180 (77.6)
	Median Survival Est. (95% CI)	5.65 (5.32, 6.77)	3.68 (3.42, 3.84)
	Hazard Ratio (95% CI)		0.575 (0.462, 0.714)
	Treatment P-value [a]		<.00001
	Interaction P-value [b]		0.02949
6 Months	Patients at Risk, Survival Est. (95% CI)	84, 0.46 (0.39, 0.53)	44, 0.25 (0.20, 0.32)
12 Months	Patients at Risk, Survival Est. (95% CI)	23, 0.26 (0.20, 0.33)	5, 0.07 (0.03, 0.13)
18 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.18 (0.11, 0.27)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table PFS1.KM.S3.FAS: Time to Progression-Free Survival on Study Therapy (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	48 (76.2)	51 (68.0)
	Median Survival Est. (95% CI)	5.39 (3.75, 5.78)	3.84 (2.99, 5.82)
	Hazard Ratio (95% CI)		0.949 (0.639, 1.408)
	Treatment P-value [a]		0.98438
	Interaction P-value [b]		0.02949
6 Months	Patients at Risk, Survival Est. (95% CI)	18, 0.36 (0.24, 0.48)	18, 0.37 (0.26, 0.49)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	3, 0.13 (0.04, 0.26)
18 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.08 (0.02, 0.21)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table PFS1.KM.S4.FAS: Time to Progression-Free Survival on Study Therapy (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	86 (68.3)	95 (73.6)
	Median Survival Est. (95% CI)	5.55 (3.91, 6.77)	3.75 (3.02, 5.13)
	Hazard Ratio (95% CI)		0.684 (0.511, 0.917)
	Treatment P-value [a]		0.01154
	Interaction P-value [b]		0.86954
6 Months	Patients at Risk, Survival Est. (95% CI)	47, 0.44 (0.35, 0.53)	29, 0.28 (0.20, 0.36)
12 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.22 (0.14, 0.31)	6, 0.14 (0.07, 0.23)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table PFS1.KM.S4.FAS: Time to Progression-Free Survival on Study Therapy (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	30 (69.8)	35 (79.5)
	Median Survival Est. (95% CI)	5.62 (3.45, 7.46)	3.35 (2.07, 5.62)
	Hazard Ratio (95% CI)		0.614 (0.377, 1.001)
	Treatment P-value [a]		0.05531
	Interaction P-value [b]		0.86954
6 Months	Patients at Risk, Survival Est. (95% CI)	16, 0.44 (0.27, 0.59)	11, 0.33 (0.18, 0.48)
12 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.24 (0.12, 0.39)	1, 0.04 (0.00, 0.15)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
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Astellas: 7465-CL-0301
Table PFS1.KM.S4.FAS: Time to Progression-Free Survival on Study Therapy (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	85 (64.4)	101 (75.4)
	Median Survival Est. (95% CI)	5.55 (5.32, 7.16)	3.71 (3.42, 5.39)
	Hazard Ratio (95% CI)		0.618 (0.463, 0.826)
	Treatment P-value [a]		0.00056
	Interaction P-value [b]		0.86954
6 Months	Patients at Risk, Survival Est. (95% CI)	39, 0.44 (0.35, 0.53)	22, 0.27 (0.19, 0.35)
12 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.20 (0.12, 0.30)	1, 0.05 (0.01, 0.12)
18 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.15 (0.07, 0.25)	1, 0.05 (0.01, 0.12)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table PFS1.KM.S5.FAS: Time to Progression-Free Survival on Study Therapy (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	71 (59.2)	86 (69.4)
	Median Survival Est. (95% CI)	6.57 (5.36, 7.66)	4.14 (3.71, 5.59)
	Hazard Ratio (95% CI)		0.623 (0.455, 0.853)
	Treatment P-value [a]		0.00248
	Interaction P-value [b]		0.81998
6 Months	Patients at Risk, Survival Est. (95% CI)	47, 0.51 (0.42, 0.60)	27, 0.33 (0.24, 0.43)
12 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.31 (0.22, 0.42)	5, 0.12 (0.05, 0.22)
18 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.24 (0.14, 0.35)	1, 0.05 (0.01, 0.17)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table PFS1.KM.S5.FAS: Time to Progression-Free Survival on Study Therapy (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	130 (71.8)	145 (79.2)
	Median Survival Est. (95% CI)	5.39 (3.94, 5.62)	3.35 (2.23, 3.78)
	Hazard Ratio (95% CI)		0.652 (0.514, 0.827)
	Treatment P-value [a]		0.00057
	Interaction P-value [b]		0.81998
6 Months	Patients at Risk, Survival Est. (95% CI)	55, 0.39 (0.31, 0.46)	35, 0.25 (0.18, 0.32)
12 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.16 (0.10, 0.23)	3, 0.05 (0.02, 0.12)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table PFS1.KM.S6.FAS: Time to Progression-Free Survival on Study Therapy (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	71 (76.3)	75 (78.9)
	Median Survival Est. (95% CI)	4.14 (3.71, 5.55)	2.63 (2.07, 3.55)
	Hazard Ratio (95% CI)		0.590 (0.425, 0.818)
	Treatment P-value [a]		0.00210
	Interaction P-value [b]		0.64639
6 Months	Patients at Risk, Survival Est. (95% CI)	26, 0.35 (0.25, 0.45)	8, 0.14 (0.07, 0.22)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.09 (0.03, 0.19)	2, 0.09 (0.04, 0.18)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

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Table PFS1.KM.S6.FAS: Time to Progression-Free Survival on Study Therapy (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	130 (62.5)	156 (73.6)
	Median Survival Est. (95% CI)	5.78 (5.49, 7.16)	4.14 (3.68, 5.55)
	Hazard Ratio (95% CI)		0.648 (0.513, 0.818)
	Treatment P-value [a]		0.00024
	Interaction P-value [b]		0.64639
6 Months	Patients at Risk, Survival Est. (95% CI)	76, 0.48 (0.40, 0.55)	54, 0.35 (0.28, 0.42)
12 Months	Patients at Risk, Survival Est. (95% CI)	21, 0.27 (0.20, 0.35)	6, 0.08 (0.04, 0.15)
18 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.22 (0.14, 0.30)	1, 0.03 (0.00, 0.11)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Table PFS1.KM.S7.FAS: Time to Progression-Free Survival on Study Therapy (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	96 (68.1)	90 (80.4)
	Median Survival Est. (95% CI)	5.55 (4.44, 7.16)	3.65 (3.35, 5.13)
	Hazard Ratio (95% CI)		0.632 (0.474, 0.843)
	Treatment P-value [a]		0.00138
	Interaction P-value [b]		0.20966
6 Months	Patients at Risk, Survival Est. (95% CI)	48, 0.44 (0.35, 0.53)	23, 0.28 (0.20, 0.37)
12 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.21 (0.13, 0.29)	2, 0.06 (0.01, 0.14)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.16 (0.09, 0.25)	1, 0.03 (0.00, 0.11)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

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Table PFS1.KM.S7.FAS: Time to Progression-Free Survival on Study Therapy (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	56 (64.4)	87 (74.4)
	Median Survival Est. (95% CI)	5.68 (3.94, 7.23)	3.25 (2.20, 3.84)
	Hazard Ratio (95% CI)		0.532 (0.380, 0.746)
	Treatment P-value [a]		0.00028
	Interaction P-value [b]		0.20966
6 Months	Patients at Risk, Survival Est. (95% CI)	32, 0.48 (0.36, 0.58)	19, 0.25 (0.17, 0.35)
12 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.25 (0.14, 0.36)	1, 0.03 (0.00, 0.13)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.16 (0.06, 0.30)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

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Table PFS1.KM.S7.FAS: Time to Progression-Free Survival on Study Therapy (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	49 (67.1)	54 (69.2)
	Median Survival Est. (95% CI)	5.55 (3.84, 6.57)	4.14 (3.68, 5.62)
	Hazard Ratio (95% CI)		0.844 (0.573, 1.243)
	Treatment P-value [a]		0.35112
	Interaction P-value [b]		0.20966
6 Months	Patients at Risk, Survival Est. (95% CI)	22, 0.39 (0.27, 0.51)	20, 0.32 (0.22, 0.44)
12 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.21 (0.11, 0.34)	5, 0.18 (0.09, 0.30)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table PFS1.KM.S8.FAS: Time to Progression-Free Survival on Study Therapy (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	63 (64.3)	74 (69.2)
	Median Survival Est. (95% CI)	5.62 (5.32, 7.29)	3.78 (2.23, 5.39)
	Hazard Ratio (95% CI)		0.702 (0.501, 0.982)
	Treatment P-value [a]		0.05162
	Interaction P-value [b]		0.51554
6 Months	Patients at Risk, Survival Est. (95% CI)	36, 0.48 (0.38, 0.58)	26, 0.34 (0.25, 0.44)
12 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.23 (0.14, 0.35)	6, 0.16 (0.08, 0.26)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.18 (0.09, 0.29)	1, 0.08 (0.01, 0.24)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

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Table PFS1.KM.S8.FAS: Time to Progression-Free Survival on Study Therapy (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	138 (68.0)	157 (78.5)
	Median Survival Est. (95% CI)	5.55 (4.44, 5.78)	3.68 (3.38, 3.84)
	Hazard Ratio (95% CI)		0.613 (0.487, 0.772)
	Treatment P-value [a]		0.00002
	Interaction P-value [b]		0.51554
6 Months	Patients at Risk, Survival Est. (95% CI)	66, 0.42 (0.35, 0.49)	36, 0.25 (0.19, 0.32)
12 Months	Patients at Risk, Survival Est. (95% CI)	15, 0.21 (0.15, 0.28)	2, 0.05 (0.02, 0.11)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.13 (0.06, 0.24)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table PFS1.KM.S9.FAS: Time to Progression-Free Survival on Study Therapy (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	175 (66.8)	203 (75.2)
	Median Survival Est. (95% CI)	5.55 (5.29, 6.08)	3.75 (3.52, 3.98)
	Hazard Ratio (95% CI)		0.639 (0.522, 0.783)
	Treatment P-value [a]		0.00001
	Interaction P-value [b]		0.80402
6 Months	Patients at Risk, Survival Est. (95% CI)	90, 0.44 (0.38, 0.50)	55, 0.28 (0.23, 0.34)
12 Months	Patients at Risk, Survival Est. (95% CI)	21, 0.22 (0.16, 0.29)	7, 0.09 (0.05, 0.14)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.16 (0.10, 0.24)	1, 0.02 (0.00, 0.10)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

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Table PFS1.KM.S9.FAS: Time to Progression-Free Survival on Study Therapy (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	26 (66.7)	28 (75.7)
	Median Survival Est. (95% CI)	5.55 (3.71, 7.20)	3.61 (2.10, 5.68)
	Hazard Ratio (95% CI)		0.687 (0.403, 1.173)
	Treatment P-value [a]		0.14675
	Interaction P-value [b]		0.80402
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.45 (0.27, 0.60)	7, 0.27 (0.13, 0.43)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.19 (0.07, 0.37)	1, 0.07 (0.01, 0.24)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.10 (0.01, 0.31)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table PFS1.KM.S10.FAS: Time to Progression-Free Survival on Study Therapy (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	32 (52.5)	36 (72.0)
	Median Survival Est. (95% CI)	7.16 (5.65, 11.10)	5.39 (3.25, 5.59)
	Hazard Ratio (95% CI)		0.514 (0.319, 0.828)
	Treatment P-value [a]		0.00518
	Interaction P-value [b]		0.26932
6 Months	Patients at Risk, Survival Est. (95% CI)	24, 0.59 (0.44, 0.71)	13, 0.35 (0.21, 0.50)
12 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.34 (0.20, 0.49)	1, 0.04 (0.00, 0.18)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table PFS1.KM.S10.FAS: Time to Progression-Free Survival on Study Therapy (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	146 (70.5)	160 (74.4)
	Median Survival Est. (95% CI)	5.42 (4.44, 5.65)	3.65 (3.35, 3.84)
	Hazard Ratio (95% CI)		0.692 (0.552, 0.867)
	Treatment P-value [a]		0.00159
	Interaction P-value [b]		0.26932
6 Months	Patients at Risk, Survival Est. (95% CI)	67, 0.40 (0.33, 0.47)	40, 0.27 (0.21, 0.34)
12 Months	Patients at Risk, Survival Est. (95% CI)	15, 0.18 (0.12, 0.25)	7, 0.10 (0.05, 0.16)
18 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.13 (0.06, 0.21)	1, 0.03 (0.00, 0.11)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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2.1.2 Sensitivitätsanalyse

Astellas: 7465-CL-0301
Table PFS1S.KM.S1.FAS: Time to Progression-Free Survival on Study Therapy (Months) - Sensitivity Analysis (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	77 (71.3)	80 (72.1)
	Median Survival Est. (95% CI)	5.45 (4.44, 6.34)	3.55 (2.37, 3.84)
	Hazard Ratio (95% CI)		0.699 (0.511, 0.956)
	Treatment P-value [a]		0.02901
	Interaction P-value [b]		0.53884
6 Months	Patients at Risk, Survival Est. (95% CI)	38, 0.43 (0.33, 0.53)	23, 0.27 (0.19, 0.37)
12 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.18 (0.10, 0.28)	1, 0.05 (0.01, 0.17)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.15 (0.08, 0.25)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
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Astellas: 7465-CL-0301
Table PFS1S.KM.S1.FAS: Time to Progression-Free Survival on Study Therapy (Months) - Sensitivity Analysis (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	127 (65.8)	154 (78.6)
	Median Survival Est. (95% CI)	5.65 (5.32, 7.20)	3.84 (3.52, 5.13)
	Hazard Ratio (95% CI)		0.618 (0.488, 0.783)
	Treatment P-value [a]		0.00005
	Interaction P-value [b]		0.53884
6 Months	Patients at Risk, Survival Est. (95% CI)	66, 0.45 (0.37, 0.52)	41, 0.29 (0.23, 0.36)
12 Months	Patients at Risk, Survival Est. (95% CI)	16, 0.23 (0.16, 0.31)	7, 0.09 (0.05, 0.15)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.16 (0.09, 0.25)	1, 0.03 (0.00, 0.10)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table PFS1S.KM.S2.FAS: Time to Progression-Free Survival on Study Therapy (Months) - Sensitivity Analysis (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	169 (67.9)	181 (75.7)
	Median Survival Est. (95% CI)	5.62 (5.36, 6.34)	3.68 (3.32, 3.94)
	Hazard Ratio (95% CI)		0.601 (0.487, 0.743)
	Treatment P-value [a]		<.00001
	Interaction P-value [b]		0.10844
6 Months	Patients at Risk, Survival Est. (95% CI)	91, 0.45 (0.38, 0.51)	48, 0.27 (0.21, 0.34)
12 Months	Patients at Risk, Survival Est. (95% CI)	22, 0.23 (0.17, 0.29)	5, 0.07 (0.03, 0.13)
18 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.18 (0.12, 0.25)	1, 0.03 (0.00, 0.12)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table PFS1S.KM.S2.FAS: Time to Progression-Free Survival on Study Therapy (Months) - Sensitivity Analysis (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	35 (67.3)	53 (77.9)
	Median Survival Est. (95% CI)	5.42 (3.71, 7.20)	4.14 (3.52, 5.62)
	Hazard Ratio (95% CI)		0.888 (0.580, 1.362)
	Treatment P-value [a]		0.61207
	Interaction P-value [b]		0.10844
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.40 (0.25, 0.54)	16, 0.33 (0.21, 0.45)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.13 (0.04, 0.27)	3, 0.12 (0.04, 0.22)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table PFS1S.KM.S3.FAS: Time to Progression-Free Survival on Study Therapy (Months) - Sensitivity Analysis (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	154 (64.7)	182 (78.4)
	Median Survival Est. (95% CI)	5.65 (5.32, 6.77)	3.68 (3.42, 3.94)
	Hazard Ratio (95% CI)		0.575 (0.463, 0.714)
	Treatment P-value [a]		<.00001
	Interaction P-value [b]		0.02744
6 Months	Patients at Risk, Survival Est. (95% CI)	85, 0.47 (0.40, 0.53)	45, 0.26 (0.20, 0.32)
12 Months	Patients at Risk, Survival Est. (95% CI)	23, 0.26 (0.19, 0.32)	5, 0.07 (0.03, 0.13)
18 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.18 (0.11, 0.26)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table PFS1S.KM.S3.FAS: Time to Progression-Free Survival on Study Therapy (Months) - Sensitivity Analysis (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	50 (79.4)	52 (69.3)
	Median Survival Est. (95% CI)	5.39 (3.75, 5.78)	3.94 (2.99, 7.23)
	Hazard Ratio (95% CI)		0.949 (0.643, 1.400)
	Treatment P-value [a]		0.97682
	Interaction P-value [b]		0.02744
6 Months	Patients at Risk, Survival Est. (95% CI)	19, 0.36 (0.24, 0.48)	19, 0.38 (0.27, 0.50)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	3, 0.12 (0.04, 0.25)
18 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.08 (0.02, 0.21)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table PFS1S.KM.S4.FAS: Time to Progression-Free Survival on Study Therapy (Months) - Sensitivity Analysis (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	88 (69.8)	96 (74.4)
	Median Survival Est. (95% CI)	5.55 (3.91, 6.77)	3.75 (3.02, 5.13)
	Hazard Ratio (95% CI)		0.686 (0.514, 0.917)
	Treatment P-value [a]		0.01158
	Interaction P-value [b]		0.86356
6 Months	Patients at Risk, Survival Est. (95% CI)	48, 0.44 (0.35, 0.53)	29, 0.28 (0.20, 0.36)
12 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.22 (0.14, 0.30)	6, 0.14 (0.07, 0.23)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table PFS1S.KM.S4.FAS: Time to Progression-Free Survival on Study Therapy (Months) - Sensitivity Analysis (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	31 (72.1)	35 (79.5)
	Median Survival Est. (95% CI)	5.65 (3.45, 7.46)	3.35 (2.07, 5.62)
	Hazard Ratio (95% CI)		0.609 (0.375, 0.989)
	Treatment P-value [a]		0.05059
	Interaction P-value [b]		0.86356
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.45 (0.29, 0.60)	11, 0.33 (0.18, 0.48)
12 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.23 (0.11, 0.38)	1, 0.04 (0.00, 0.15)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table PFS1S.KM.S4.FAS: Time to Progression-Free Survival on Study Therapy (Months) - Sensitivity Analysis (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	85 (64.4)	103 (76.9)
	Median Survival Est. (95% CI)	5.55 (5.32, 7.16)	3.78 (3.52, 5.39)
	Hazard Ratio (95% CI)		0.621 (0.466, 0.829)
	Treatment P-value [a]		0.00062
	Interaction P-value [b]		0.86356
6 Months	Patients at Risk, Survival Est. (95% CI)	39, 0.44 (0.35, 0.53)	24, 0.28 (0.20, 0.37)
12 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.20 (0.12, 0.30)	1, 0.04 (0.01, 0.12)
18 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.15 (0.07, 0.25)	1, 0.04 (0.01, 0.12)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table PFS1S.KM.S5.FAS: Time to Progression-Free Survival on Study Therapy (Months) - Sensitivity Analysis (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	72 (60.0)	86 (69.4)
	Median Survival Est. (95% CI)	6.57 (5.55, 7.66)	4.14 (3.71, 5.59)
	Hazard Ratio (95% CI)		0.622 (0.455, 0.851)
	Treatment P-value [a]		0.00237
	Interaction P-value [b]		0.78317
6 Months	Patients at Risk, Survival Est. (95% CI)	48, 0.52 (0.42, 0.61)	27, 0.33 (0.24, 0.43)
12 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.31 (0.21, 0.41)	5, 0.12 (0.05, 0.22)
18 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.23 (0.14, 0.34)	1, 0.05 (0.01, 0.17)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table PFS1S.KM.S5.FAS: Time to Progression-Free Survival on Study Therapy (Months) - Sensitivity Analysis (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	132 (72.9)	148 (80.9)
	Median Survival Est. (95% CI)	5.39 (3.94, 5.62)	3.35 (2.30, 3.84)
	Hazard Ratio (95% CI)		0.657 (0.519, 0.832)
	Treatment P-value [a]		0.00065
	Interaction P-value [b]		0.78317
6 Months	Patients at Risk, Survival Est. (95% CI)	56, 0.39 (0.32, 0.46)	37, 0.26 (0.19, 0.33)
12 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.15 (0.10, 0.22)	3, 0.05 (0.02, 0.11)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table PFS1S.KM.S6.FAS: Time to Progression-Free Survival on Study Therapy (Months) - Sensitivity Analysis (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	73 (78.5)	76 (80.0)
	Median Survival Est. (95% CI)	4.44 (3.71, 5.55)	2.63 (2.07, 3.55)
	Hazard Ratio (95% CI)		0.592 (0.428, 0.818)
	Treatment P-value [a]		0.00183
	Interaction P-value [b]		0.65399
6 Months	Patients at Risk, Survival Est. (95% CI)	27, 0.35 (0.25, 0.46)	9, 0.15 (0.08, 0.23)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.08 (0.03, 0.18)	2, 0.09 (0.03, 0.17)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table PFS1S.KM.S6.FAS: Time to Progression-Free Survival on Study Therapy (Months) - Sensitivity Analysis (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	131 (63.0)	158 (74.5)
	Median Survival Est. (95% CI)	5.78 (5.49, 7.20)	4.14 (3.68, 5.55)
	Hazard Ratio (95% CI)		0.648 (0.514, 0.818)
	Treatment P-value [a]		0.00023
	Interaction P-value [b]		0.65399
6 Months	Patients at Risk, Survival Est. (95% CI)	77, 0.48 (0.41, 0.55)	55, 0.35 (0.28, 0.42)
12 Months	Patients at Risk, Survival Est. (95% CI)	21, 0.27 (0.20, 0.34)	6, 0.08 (0.04, 0.15)
18 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.21 (0.14, 0.29)	1, 0.03 (0.00, 0.11)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table PFS1S.KM.S7.FAS: Time to Progression-Free Survival on Study Therapy (Months) - Sensitivity Analysis (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	97 (68.8)	90 (80.4)
	Median Survival Est. (95% CI)	5.55 (4.44, 7.20)	3.65 (3.35, 5.13)
	Hazard Ratio (95% CI)		0.629 (0.472, 0.839)
	Treatment P-value [a]		0.00123
	Interaction P-value [b]		0.20868
6 Months	Patients at Risk, Survival Est. (95% CI)	49, 0.45 (0.36, 0.53)	23, 0.28 (0.20, 0.37)
12 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.20 (0.13, 0.29)	2, 0.06 (0.01, 0.14)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.16 (0.09, 0.25)	1, 0.03 (0.00, 0.11)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table PFS1S.KM.S7.FAS: Time to Progression-Free Survival on Study Therapy (Months) - Sensitivity Analysis (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	56 (64.4)	89 (76.1)
	Median Survival Est. (95% CI)	5.68 (3.94, 7.23)	3.38 (2.20, 3.84)
	Hazard Ratio (95% CI)		0.537 (0.384, 0.752)
	Treatment P-value [a]		0.00031
	Interaction P-value [b]		0.20868
6 Months	Patients at Risk, Survival Est. (95% CI)	32, 0.48 (0.36, 0.58)	21, 0.27 (0.18, 0.36)
12 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.25 (0.14, 0.36)	1, 0.03 (0.00, 0.12)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.16 (0.06, 0.30)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table PFS1S.KM.S7.FAS: Time to Progression-Free Survival on Study Therapy (Months) - Sensitivity Analysis (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	51 (69.9)	55 (70.5)
	Median Survival Est. (95% CI)	5.55 (4.60, 6.57)	4.16 (3.71, 5.55)
	Hazard Ratio (95% CI)		0.847 (0.579, 1.241)
	Treatment P-value [a]		0.35449
	Interaction P-value [b]		0.20868
6 Months	Patients at Risk, Survival Est. (95% CI)	23, 0.39 (0.28, 0.51)	20, 0.32 (0.21, 0.43)
12 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.20 (0.10, 0.33)	5, 0.18 (0.09, 0.29)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table PFS1S.KM.S8.FAS: Time to Progression-Free Survival on Study Therapy (Months) - Sensitivity Analysis (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	65 (66.3)	74 (69.2)
	Median Survival Est. (95% CI)	5.62 (5.32, 7.29)	3.78 (2.23, 5.39)
	Hazard Ratio (95% CI)		0.704 (0.504, 0.983)
	Treatment P-value [a]		0.05194
	Interaction P-value [b]		0.51395
6 Months	Patients at Risk, Survival Est. (95% CI)	37, 0.48 (0.38, 0.58)	26, 0.34 (0.25, 0.44)
12 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.23 (0.13, 0.34)	6, 0.16 (0.08, 0.26)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.17 (0.08, 0.28)	1, 0.08 (0.01, 0.24)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table PFS1S.KM.S8.FAS: Time to Progression-Free Survival on Study Therapy (Months) - Sensitivity Analysis (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	139 (68.5)	160 (80.0)
	Median Survival Est. (95% CI)	5.55 (4.44, 5.78)	3.68 (3.42, 4.04)
	Hazard Ratio (95% CI)		0.616 (0.490, 0.774)
	Treatment P-value [a]		0.00002
	Interaction P-value [b]		0.51395
6 Months	Patients at Risk, Survival Est. (95% CI)	67, 0.42 (0.35, 0.49)	38, 0.26 (0.20, 0.33)
12 Months	Patients at Risk, Survival Est. (95% CI)	15, 0.21 (0.14, 0.28)	2, 0.05 (0.02, 0.10)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.13 (0.06, 0.24)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table PFS1S.KM.S9.FAS: Time to Progression-Free Survival on Study Therapy (Months) - Sensitivity Analysis (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	178 (67.9)	206 (76.3)
	Median Survival Est. (95% CI)	5.55 (5.32, 6.08)	3.75 (3.52, 4.07)
	Hazard Ratio (95% CI)		0.641 (0.524, 0.784)
	Treatment P-value [a]		0.00001
	Interaction P-value [b]		0.81764
6 Months	Patients at Risk, Survival Est. (95% CI)	92, 0.44 (0.38, 0.50)	57, 0.29 (0.23, 0.35)
12 Months	Patients at Risk, Survival Est. (95% CI)	21, 0.22 (0.16, 0.28)	7, 0.08 (0.05, 0.14)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.16 (0.09, 0.23)	1, 0.02 (0.00, 0.10)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table PFS1S.KM.S9.FAS: Time to Progression-Free Survival on Study Therapy (Months) - Sensitivity Analysis (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	26 (66.7)	28 (75.7)
	Median Survival Est. (95% CI)	5.55 (3.71, 7.20)	3.61 (2.10, 5.68)
	Hazard Ratio (95% CI)		0.686 (0.402, 1.170)
	Treatment P-value [a]		0.14675
	Interaction P-value [b]		0.81764
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.45 (0.27, 0.60)	7, 0.27 (0.13, 0.43)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.19 (0.07, 0.37)	1, 0.07 (0.01, 0.24)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.10 (0.01, 0.31)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table PFS1S.KM.S10.FAS: Time to Progression-Free Survival on Study Therapy (Months) - Sensitivity Analysis (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	33 (54.1)	37 (74.0)
	Median Survival Est. (95% CI)	7.23 (5.78, 11.10)	5.39 (3.65, 7.23)
	Hazard Ratio (95% CI)		0.523 (0.327, 0.836)
	Treatment P-value [a]		0.00607
	Interaction P-value [b]		0.29636
6 Months	Patients at Risk, Survival Est. (95% CI)	25, 0.60 (0.45, 0.72)	14, 0.37 (0.22, 0.51)
12 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.33 (0.19, 0.48)	1, 0.04 (0.00, 0.17)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table PFS1S.KM.S10.FAS: Time to Progression-Free Survival on Study Therapy (Months) - Sensitivity Analysis (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	147 (71.0)	162 (75.3)
	Median Survival Est. (95% CI)	5.45 (4.60, 5.65)	3.68 (3.35, 3.94)
	Hazard Ratio (95% CI)		0.690 (0.551, 0.863)
	Treatment P-value [a]		0.00141
	Interaction P-value [b]		0.29636
6 Months	Patients at Risk, Survival Est. (95% CI)	68, 0.41 (0.33, 0.47)	41, 0.27 (0.21, 0.34)
12 Months	Patients at Risk, Survival Est. (95% CI)	15, 0.18 (0.12, 0.25)	7, 0.10 (0.05, 0.16)
18 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.12 (0.06, 0.21)	1, 0.03 (0.00, 0.11)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
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2.2 Subgruppenanalysen zum Progressionsfreien Überleben 2 (PFS2)

Astellas: 7465-CL-0301
Table PFS2.KM.S1.FAS: Time to Progression-Free Survival After Next-line Therapy (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	55 (50.9)	79 (71.2)
	Median Survival Est. (95% CI)	9.89 (7.13, 11.40)	6.70 (5.95, 8.05)
	Hazard Ratio (95% CI)		0.626 (0.444, 0.884)
	Treatment P-value [a]		0.00879
	Interaction P-value [b]		0.87110
6 Months	Patients at Risk, Survival Est. (95% CI)	68, 0.71 (0.62, 0.79)	57, 0.58 (0.48, 0.67)
12 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.34 (0.22, 0.47)	9, 0.17 (0.10, 0.27)
18 Months	Patients at Risk, Survival Est. (95% CI)	0	2, 0.12 (0.05, 0.22)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table PFS2.KM.S1.FAS: Time to Progression-Free Survival After Next-line Therapy (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	97 (50.3)	116 (59.2)
	Median Survival Est. (95% CI)	9.63 (8.08, 11.27)	7.23 (6.51, 8.71)
	Hazard Ratio (95% CI)		0.649 (0.495, 0.852)
	Treatment P-value [a]		0.00189
	Interaction P-value [b]		0.87110
6 Months	Patients at Risk, Survival Est. (95% CI)	116, 0.71 (0.64, 0.77)	99, 0.65 (0.57, 0.71)
12 Months	Patients at Risk, Survival Est. (95% CI)	32, 0.39 (0.31, 0.48)	19, 0.28 (0.20, 0.36)
18 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.26 (0.15, 0.39)	1, 0.05 (0.01, 0.17)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
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Astellas: 7465-CL-0301
Table PFS2.KM.S2.FAS: Time to Progression-Free Survival After Next-line Therapy (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	123 (49.4)	152 (63.6)
	Median Survival Est. (95% CI)	9.99 (8.08, 11.56)	7.03 (6.41, 8.15)
	Hazard Ratio (95% CI)		0.592 (0.466, 0.751)
	Treatment P-value [a]		0.00002
	Interaction P-value [b]		0.10641
6 Months	Patients at Risk, Survival Est. (95% CI)	158, 0.72 (0.66, 0.78)	120, 0.61 (0.54, 0.67)
12 Months	Patients at Risk, Survival Est. (95% CI)	38, 0.41 (0.33, 0.48)	20, 0.23 (0.16, 0.30)
18 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.26 (0.15, 0.39)	3, 0.09 (0.03, 0.18)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table PFS2.KM.S2.FAS: Time to Progression-Free Survival After Next-line Therapy (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	29 (55.8)	43 (63.2)
	Median Survival Est. (95% CI)	8.48 (5.59, 9.92)	7.00 (6.05, 8.94)
	Hazard Ratio (95% CI)		0.914 (0.571, 1.464)
	Treatment P-value [a]		0.71119
	Interaction P-value [b]		0.10641
6 Months	Patients at Risk, Survival Est. (95% CI)	26, 0.66 (0.49, 0.78)	36, 0.66 (0.53, 0.77)
12 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.23 (0.10, 0.39)	8, 0.27 (0.15, 0.40)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.11 (0.01, 0.35)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table PFS2.KM.S3.FAS: Time to Progression-Free Survival After Next-line Therapy (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	117 (49.2)	152 (65.5)
	Median Survival Est. (95% CI)	9.63 (7.95, 10.81)	7.00 (6.41, 8.05)
	Hazard Ratio (95% CI)		0.574 (0.450, 0.732)
	Treatment P-value [a]		<.00001
	Interaction P-value [b]		0.07996
6 Months	Patients at Risk, Survival Est. (95% CI)	149, 0.73 (0.66, 0.78)	118, 0.61 (0.54, 0.67)
12 Months	Patients at Risk, Survival Est. (95% CI)	37, 0.40 (0.32, 0.48)	20, 0.21 (0.15, 0.28)
18 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.28 (0.17, 0.40)	1, 0.06 (0.02, 0.14)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table PFS2.KM.S3.FAS: Time to Progression-Free Survival After Next-line Therapy (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	35 (55.6)	43 (57.3)
	Median Survival Est. (95% CI)	9.46 (6.34, 11.63)	7.36 (6.24, 10.68)
	Hazard Ratio (95% CI)		0.908 (0.580, 1.421)
	Treatment P-value [a]		0.73291
	Interaction P-value [b]		0.07996
6 Months	Patients at Risk, Survival Est. (95% CI)	35, 0.66 (0.53, 0.77)	38, 0.65 (0.52, 0.75)
12 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.29 (0.15, 0.45)	8, 0.31 (0.18, 0.45)
18 Months	Patients at Risk, Survival Est. (95% CI)	0	2, 0.17 (0.04, 0.36)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table PFS2.KM.S4.FAS: Time to Progression-Free Survival After Next-line Therapy (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	66 (52.4)	79 (61.2)
	Median Survival Est. (95% CI)	8.28 (7.20, 10.41)	6.67 (5.98, 8.05)
	Hazard Ratio (95% CI)		0.642 (0.463, 0.890)
	Treatment P-value [a]		0.01264
	Interaction P-value [b]		0.94559
6 Months	Patients at Risk, Survival Est. (95% CI)	79, 0.72 (0.63, 0.79)	59, 0.59 (0.49, 0.68)
12 Months	Patients at Risk, Survival Est. (95% CI)	16, 0.38 (0.28, 0.48)	11, 0.25 (0.16, 0.35)
18 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.10 (0.02, 0.24)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table PFS2.KM.S4.FAS: Time to Progression-Free Survival After Next-line Therapy (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	26 (60.5)	30 (68.2)
	Median Survival Est. (95% CI)	9.59 (6.77, 17.15)	7.10 (4.93, 11.40)
	Hazard Ratio (95% CI)		0.681 (0.400, 1.157)
	Treatment P-value [a]		0.16654
	Interaction P-value [b]		0.94559
6 Months	Patients at Risk, Survival Est. (95% CI)	27, 0.70 (0.53, 0.81)	23, 0.59 (0.42, 0.73)
12 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.36 (0.21, 0.52)	8, 0.33 (0.18, 0.49)
18 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.30 (0.15, 0.47)	1, 0.08 (0.01, 0.28)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table PFS2.KM.S4.FAS: Time to Progression-Free Survival After Next-line Therapy (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	60 (45.5)	86 (64.2)
	Median Survival Est. (95% CI)	10.15 (8.61, 11.83)	7.62 (6.64, 8.61)
	Hazard Ratio (95% CI)		0.613 (0.441, 0.854)
	Treatment P-value [a]		0.00217
	Interaction P-value [b]		0.94559
6 Months	Patients at Risk, Survival Est. (95% CI)	78, 0.71 (0.62, 0.79)	74, 0.66 (0.57, 0.74)
12 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.38 (0.27, 0.50)	9, 0.18 (0.10, 0.28)
18 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.23 (0.11, 0.38)	1, 0.07 (0.02, 0.18)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table PFS2.KM.S5.FAS: Time to Progression-Free Survival After Next-line Therapy (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	50 (41.7)	67 (54.0)
	Median Survival Est. (95% CI)	10.58 (9.26, 15.34)	8.84 (7.36, 9.59)
	Hazard Ratio (95% CI)		0.693 (0.480, 1.000)
	Treatment P-value [a]		0.03597
	Interaction P-value [b]		0.46851
6 Months	Patients at Risk, Survival Est. (95% CI)	81, 0.81 (0.72, 0.87)	82, 0.81 (0.73, 0.88)
12 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.40 (0.28, 0.52)	12, 0.27 (0.17, 0.38)
18 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.35 (0.22, 0.49)	2, 0.17 (0.08, 0.30)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table PFS2.KM.S5.FAS: Time to Progression-Free Survival After Next-line Therapy (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	102 (56.4)	128 (69.9)
	Median Survival Est. (95% CI)	8.25 (6.80, 9.89)	5.98 (4.83, 6.67)
	Hazard Ratio (95% CI)		0.586 (0.451, 0.762)
	Treatment P-value [a]		0.00017
	Interaction P-value [b]		0.46851
6 Months	Patients at Risk, Survival Est. (95% CI)	103, 0.65 (0.57, 0.72)	74, 0.49 (0.41, 0.57)
12 Months	Patients at Risk, Survival Est. (95% CI)	26, 0.36 (0.28, 0.44)	16, 0.21 (0.14, 0.29)
18 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.20 (0.10, 0.33)	1, 0.03 (0.00, 0.12)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

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Table PFS2.KM.S6.FAS: Time to Progression-Free Survival After Next-line Therapy (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	57 (61.3)	67 (70.5)
	Median Survival Est. (95% CI)	7.85 (5.59, 9.26)	5.78 (4.40, 6.05)
	Hazard Ratio (95% CI)		0.578 (0.405, 0.826)
	Treatment P-value [a]		0.00804
	Interaction P-value [b]		0.66630
6 Months	Patients at Risk, Survival Est. (95% CI)	43, 0.56 (0.45, 0.66)	32, 0.43 (0.32, 0.54)
12 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.24 (0.14, 0.36)	4, 0.12 (0.05, 0.23)
18 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.21 (0.10, 0.33)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

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Table PFS2.KM.S6.FAS: Time to Progression-Free Survival After Next-line Therapy (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	95 (45.7)	128 (60.4)
	Median Survival Est. (95% CI)	10.15 (8.48, 14.42)	8.31 (7.10, 9.17)
	Hazard Ratio (95% CI)		0.638 (0.489, 0.832)
	Treatment P-value [a]		0.00076
	Interaction P-value [b]		0.66630
6 Months	Patients at Risk, Survival Est. (95% CI)	141, 0.78 (0.71, 0.83)	124, 0.71 (0.64, 0.77)
12 Months	Patients at Risk, Survival Est. (95% CI)	35, 0.44 (0.35, 0.52)	24, 0.28 (0.21, 0.36)
18 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.26 (0.13, 0.41)	3, 0.10 (0.04, 0.20)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table PFS2.KM.S7.FAS: Time to Progression-Free Survival After Next-line Therapy (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	70 (49.6)	68 (60.7)
	Median Survival Est. (95% CI)	9.89 (7.62, 13.01)	6.47 (5.78, 8.51)
	Hazard Ratio (95% CI)		0.590 (0.422, 0.826)
	Treatment P-value [a]		0.00342
	Interaction P-value [b]		0.76587
6 Months	Patients at Risk, Survival Est. (95% CI)	85, 0.71 (0.63, 0.78)	49, 0.57 (0.47, 0.66)
12 Months	Patients at Risk, Survival Est. (95% CI)	23, 0.40 (0.30, 0.50)	11, 0.25 (0.16, 0.36)
18 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.21 (0.06, 0.41)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table PFS2.KM.S7.FAS: Time to Progression-Free Survival After Next-line Therapy (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	46 (52.9)	83 (70.9)
	Median Survival Est. (95% CI)	9.63 (7.52, 11.63)	7.23 (6.64, 8.61)
	Hazard Ratio (95% CI)		0.638 (0.444, 0.915)
	Treatment P-value [a]		0.01438
	Interaction P-value [b]		0.76587
6 Months	Patients at Risk, Survival Est. (95% CI)	53, 0.70 (0.58, 0.79)	66, 0.65 (0.55, 0.74)
12 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.33 (0.21, 0.46)	11, 0.21 (0.13, 0.30)
18 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.25 (0.12, 0.40)	3, 0.09 (0.03, 0.19)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

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Table PFS2.KM.S7.FAS: Time to Progression-Free Survival After Next-line Therapy (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	36 (49.3)	44 (56.4)
	Median Survival Est. (95% CI)	8.44 (7.49, 14.13)	7.43 (6.21, 9.46)
	Hazard Ratio (95% CI)		0.725 (0.467, 1.127)
	Treatment P-value [a]		0.15609
	Interaction P-value [b]		0.76587
6 Months	Patients at Risk, Survival Est. (95% CI)	46, 0.73 (0.61, 0.82)	41, 0.64 (0.52, 0.74)
12 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.39 (0.25, 0.52)	6, 0.27 (0.14, 0.41)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table PFS2.KM.S8.FAS: Time to Progression-Free Survival After Next-line Therapy (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	47 (48.0)	62 (57.9)
	Median Survival Est. (95% CI)	9.99 (8.28, 13.01)	7.89 (6.28, 9.53)
	Hazard Ratio (95% CI)		0.673 (0.461, 0.984)
	Treatment P-value [a]		0.04389
	Interaction P-value [b]		0.72224
6 Months	Patients at Risk, Survival Est. (95% CI)	62, 0.71 (0.61, 0.80)	59, 0.67 (0.56, 0.75)
12 Months	Patients at Risk, Survival Est. (95% CI)	14, 0.38 (0.26, 0.51)	10, 0.30 (0.19, 0.41)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.25 (0.12, 0.41)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table PFS2.KM.S8.FAS: Time to Progression-Free Survival After Next-line Therapy (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	105 (51.7)	133 (66.5)
	Median Survival Est. (95% CI)	8.61 (7.59, 10.58)	6.97 (6.37, 7.79)
	Hazard Ratio (95% CI)		0.620 (0.479, 0.801)
	Treatment P-value [a]		0.00026
	Interaction P-value [b]		0.72224
6 Months	Patients at Risk, Survival Est. (95% CI)	122, 0.71 (0.64, 0.77)	97, 0.60 (0.52, 0.67)
12 Months	Patients at Risk, Survival Est. (95% CI)	29, 0.38 (0.29, 0.46)	18, 0.21 (0.14, 0.28)
18 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.25 (0.14, 0.38)	3, 0.08 (0.03, 0.17)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table PFS2.KM.S9.FAS: Time to Progression-Free Survival After Next-line Therapy (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	132 (50.4)	170 (63.0)
	Median Survival Est. (95% CI)	9.79 (8.25, 11.04)	7.00 (6.51, 8.05)
	Hazard Ratio (95% CI)		0.625 (0.497, 0.786)
	Treatment P-value [a]		0.00004
	Interaction P-value [b]		0.62595
6 Months	Patients at Risk, Survival Est. (95% CI)	161, 0.71 (0.65, 0.77)	136, 0.62 (0.56, 0.68)
12 Months	Patients at Risk, Survival Est. (95% CI)	38, 0.38 (0.30, 0.45)	25, 0.24 (0.18, 0.31)
18 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.23 (0.13, 0.35)	2, 0.06 (0.02, 0.14)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table PFS2.KM.S9.FAS: Time to Progression-Free Survival After Next-line Therapy (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	20 (51.3)	25 (67.6)
	Median Survival Est. (95% CI)	7.89 (6.41, NC)	7.36 (4.86, 10.55)
	Hazard Ratio (95% CI)		0.731 (0.406, 1.317)
	Treatment P-value [a]		0.30413
	Interaction P-value [b]		0.62595
6 Months	Patients at Risk, Survival Est. (95% CI)	23, 0.71 (0.54, 0.83)	20, 0.61 (0.43, 0.74)
12 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.38 (0.21, 0.55)	3, 0.18 (0.06, 0.37)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.38 (0.21, 0.55)	1, 0.18 (0.06, 0.37)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table PFS2.KM.S10.FAS: Time to Progression-Free Survival After Next-line Therapy (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	22 (36.1)	29 (58.0)
	Median Survival Est. (95% CI)	9.99 (8.90, NC)	8.05 (6.57, 8.87)
	Hazard Ratio (95% CI)		0.495 (0.284, 0.862)
	Treatment P-value [a]		0.00904
	Interaction P-value [b]		0.28327
6 Months	Patients at Risk, Survival Est. (95% CI)	43, 0.81 (0.68, 0.89)	29, 0.71 (0.56, 0.82)
12 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.50 (0.33, 0.65)	3, 0.21 (0.07, 0.40)
18 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.14 (0.03, 0.33)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table PFS2.KM.S10.FAS: Time to Progression-Free Survival After Next-line Therapy (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	114 (55.1)	140 (65.1)
	Median Survival Est. (95% CI)	8.48 (7.62, 10.41)	6.87 (6.28, 8.05)
	Hazard Ratio (95% CI)		0.691 (0.539, 0.885)
	Treatment P-value [a]		0.00353
	Interaction P-value [b]		0.28327
6 Months	Patients at Risk, Survival Est. (95% CI)	124, 0.70 (0.63, 0.76)	107, 0.61 (0.54, 0.68)
12 Months	Patients at Risk, Survival Est. (95% CI)	28, 0.34 (0.26, 0.42)	22, 0.24 (0.17, 0.31)
18 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.20 (0.11, 0.32)	2, 0.07 (0.02, 0.16)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
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2.3 Subgruppenanalysen zum Ansprechen

2.3.1 Gesamtansprechrate

Astellas: 7465-CL-0301
Table ORC.BIN.S1.RES: Overall Response - Confirmed (Response Evaluable Set)
Subgroup: Age Group 1

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
<65 years	N, n (%)	104, 42 (40.4)	105, 15 (14.3)	
	OR, SE (95% CI)			4.065, 0.343 (2.075, 7.963)
	Treatment P-value			0.00004
	Peto's OR (95% CI)			3.704 (2.018, 6.800)
	RR (95% CI)			2.827 (1.675, 4.772)
	Treatment P-value			0.00010
	RD (95% CI)			0.261 (0.145, 0.377)
	Treatment P-value			<.00001

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table ORC.BIN.S1.RES: Overall Response - Confirmed (Response Evaluable Set)
Subgroup: Age Group 1

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
>=65 years	N, n (%)	184, 75 (40.8)	191, 38 (19.9)	
	OR, SE (95% CI)			2.770, 0.235 (1.747, 4.394)
	Treatment P-value			0.00001
	Interaction P-value [b]			0.35361
	Peto's OR (95% CI)			2.687 (1.729, 4.175)
	RR (95% CI)			2.049 (1.468, 2.860)
	Treatment P-value			0.00003
	Interaction P-value [b]			0.30157
	RD (95% CI)			0.209 (0.118, 0.299)
	Treatment P-value			<.00001
	Interaction P-value [b]			0.48598

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table ORC.BIN.S2.RES: Overall Response - Confirmed (Response Evaluable Set)
Subgroup: Age Group 2

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
<75 years	N, n (%)	237, 102 (43.0)	230, 38 (16.5)	
	OR, SE (95% CI)			3.818, 0.221 (2.477, 5.884)
	Treatment P-value			<.00001
	Peto's OR (95% CI)			3.527 (2.375, 5.238)
	RR (95% CI)			2.605 (1.882, 3.607)
	Treatment P-value			<.00001
	RD (95% CI)			0.265 (0.186, 0.344)
	Treatment P-value			<.00001

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table ORC.BIN.S2.RES: Overall Response - Confirmed (Response Evaluable Set)
Subgroup: Age Group 2

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
>=75 years	N, n (%)	51, 15 (29.4)	66, 15 (22.7)	
	OR, SE (95% CI)			1.417, 0.425 (0.616, 3.259)
	Treatment P-value			0.41260
	Interaction P-value [b]			0.03921
	Peto's OR (95% CI)			1.416 (0.615, 3.257)
	RR (95% CI)			1.294 (0.699, 2.395)
	Treatment P-value			0.41153
	Interaction P-value [b]			0.05090
	RD (95% CI)			0.067 (-0.094, 0.228)
	Treatment P-value			0.41524
	Interaction P-value [b]			0.03174

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table ORC.BIN.S3.RES: Overall Response - Confirmed (Response Evaluable Set)
Subgroup: Gender

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
Male	N, n (%)	228, 90 (39.5)	224, 37 (16.5)	
	OR, SE (95% CI)			3.296, 0.225 (2.120, 5.125)
	Treatment P-value			<.00001
	Peto's OR (95% CI)			3.107 (2.063, 4.681)
	RR (95% CI)			2.390 (1.709, 3.342)
	Treatment P-value			<.00001
	RD (95% CI)			0.230 (0.150, 0.309)
	Treatment P-value			<.00001

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table ORC.BIN.S3.RES: Overall Response - Confirmed (Response Evaluable Set)
Subgroup: Gender

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
Female	N, n (%)	60, 27 (45.0)	72, 16 (22.2)	
	OR, SE (95% CI)			2.864, 0.384 (1.348, 6.082)
	Treatment P-value			0.00619
	Interaction P-value [b]			0.75256
	Peto's OR (95% CI)			2.799 (1.351, 5.798)
	RR (95% CI)			2.025 (1.210, 3.388)
	Treatment P-value			0.00722
	Interaction P-value [b]			0.59960
	RD (95% CI)			0.228 (0.069, 0.386)
	Treatment P-value			0.00481
	Interaction P-value [b]			0.98430

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table ORC.BIN.S4.RES: Overall Response - Confirmed (Response Evaluable Set)
Subgroup: Region

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
Western Europe	N, n (%)	117, 46 (39.3)	125, 22 (17.6)	
	OR, SE (95% CI)			3.033, 0.302 (1.679, 5.479)
	Treatment P-value			0.00023
	Peto's OR (95% CI)			2.917 (1.666, 5.105)
	RR (95% CI)			2.234 (1.437, 3.472)
	Treatment P-value			0.00036
	RD (95% CI)			0.217 (0.106, 0.328)
	Treatment P-value			0.00012

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table ORC.BIN.S4.RES: Overall Response - Confirmed (Response Evaluable Set)
Subgroup: Region

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
US	N, n (%)	43, 15 (34.9)	41, 6 (14.6)	
	OR, SE (95% CI)			3.125, 0.546 (1.073, 9.104)
	Treatment P-value			0.03674
	Peto's OR (95% CI)			2.907 (1.089, 7.762)
	RR (95% CI)			2.384 (1.024, 5.547)
	Treatment P-value			0.04381
	RD (95% CI)			0.202 (0.024, 0.381)
	Treatment P-value			0.02650

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table ORC.BIN.S4.RES: Overall Response - Confirmed (Response Evaluable Set)
Subgroup: Region

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
Rest of the World	N, n (%)	128, 56 (43.8)	130, 25 (19.2)	
	OR, SE (95% CI)			3.267, 0.285 (1.868, 5.712)
	Treatment P-value			0.00003
	Interaction P-value [b]			0.98405
	Peto's OR (95% CI)			3.108 (1.839, 5.253)
	RR (95% CI)			2.275 (1.520, 3.405)
	Treatment P-value			0.00006
	Interaction P-value [b]			0.99095
	RD (95% CI)			0.245 (0.136, 0.355)
	Treatment P-value			0.00001
	Interaction P-value [b]			0.90112

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table ORC.BIN.S5.RES: Overall Response - Confirmed (Response Evaluable Set)
Subgroup: ECOG PS from IRT Strata

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
0	N, n (%)	115, 49 (42.6)	121, 30 (24.8)	
	OR, SE (95% CI)			2.252, 0.283 (1.294, 3.919)
	Treatment P-value			0.00407
	Peto's OR (95% CI)			2.218 (1.293, 3.805)
	RR (95% CI)			1.719 (1.180, 2.503)
	Treatment P-value			0.00475
	RD (95% CI)			0.178 (0.059, 0.297)
	Treatment P-value			0.00326

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table ORC.BIN.S5.RES: Overall Response - Confirmed (Response Evaluable Set)
Subgroup: ECOG PS from IRT Strata

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
1	N, n (%)	173, 68 (39.3)	175, 23 (13.1)	
	OR, SE (95% CI)			4.280, 0.273 (2.509, 7.302)
	Treatment P-value			<.00001
	Interaction P-value [b]			0.10098
	Peto's OR (95% CI)			3.861 (2.395, 6.224)
	RR (95% CI)			2.991 (1.958, 4.568)
	Treatment P-value			<.00001
	Interaction P-value [b]			0.05333
	RD (95% CI)			0.262 (0.173, 0.350)
	Treatment P-value			<.00001
	Interaction P-value [b]			0.26756

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table ORC.BIN.S6.RES: Overall Response - Confirmed (Response Evaluable Set)
Subgroup: Liver Metastasis from IRT Strata

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
Yes	N, n (%)	93, 33 (35.5)	93, 10 (10.8)	
	OR, SE (95% CI)			4.565, 0.399 (2.089, 9.974)
	Treatment P-value			0.00014
	Peto's OR (95% CI)			3.991 (2.022, 7.877)
	RR (95% CI)			3.300 (1.729, 6.299)
	Treatment P-value			0.00030
	RD (95% CI)			0.247 (0.131, 0.363)
	Treatment P-value			0.00003

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table ORC.BIN.S6.RES: Overall Response - Confirmed (Response Evaluable Set)
Subgroup: Liver Metastasis from IRT Strata

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
No	N, n (%)	195, 84 (43.1)	203, 43 (21.2)	
	OR, SE (95% CI)			2.816, 0.225 (1.813, 4.373)
	Treatment P-value			<.00001
	Interaction P-value [b]			0.28394
	Peto's OR (95% CI)			2.732 (1.793, 4.163)
	RR (95% CI)			2.034 (1.491, 2.774)
	Treatment P-value			<.00001
	Interaction P-value [b]			0.17043
	RD (95% CI)			0.219 (0.130, 0.308)
	Treatment P-value			<.00001
	Interaction P-value [b]			0.70395

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
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Astellas: 7465-CL-0301
Table ORC.BIN.S7.RES: Overall Response - Confirmed (Response Evaluable Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
Paclitaxel	N, n (%)	134, 56 (41.8)	109, 28 (25.7)	
	OR, SE (95% CI)			2.077, 0.281 (1.198, 3.600)
	Treatment P-value			0.00920
	Peto's OR (95% CI)			2.032 (1.195, 3.454)
	RR (95% CI)			1.627 (1.116, 2.371)
	Treatment P-value			0.01133
	RD (95% CI)			0.161 (0.044, 0.278)
	Treatment P-value			0.00701

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table ORC.BIN.S7.RES: Overall Response - Confirmed (Response Evaluable Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
Docetaxel	N, n (%)	84, 33 (39.3)	112, 13 (11.6)	
	OR, SE (95% CI)			4.928, 0.370 (2.386, 10.177)
	Treatment P-value			0.00002
	Peto's OR (95% CI)			4.633 (2.381, 9.016)
	RR (95% CI)			3.385 (1.902, 6.021)
	Treatment P-value			0.00003
	RD (95% CI)			0.277 (0.157, 0.397)
	Treatment P-value			<.00001

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table ORC.BIN.S7.RES: Overall Response - Confirmed (Response Evaluable Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
Vinflunine	N, n (%)	70, 28 (40.0)	75, 12 (16.0)	
	OR, SE (95% CI)			3.500, 0.398 (1.603, 7.642)
	Treatment P-value			0.00166
	Interaction P-value [b]			0.15681
	Peto's OR (95% CI)			3.297 (1.595, 6.817)
	RR (95% CI)			2.500 (1.382, 4.522)
	Treatment P-value			0.00244
	Interaction P-value [b]			0.08976
	RD (95% CI)			0.240 (0.098, 0.382)
	Treatment P-value			0.00089
	Interaction P-value [b]			0.38179

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table ORC.BIN.S8.RES: Overall Response - Confirmed (Response Evaluable Set)
Subgroup: Primary Site of Tumor

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
Upper Tract	N, n (%)	98, 43 (43.9)	105, 20 (19.0)	
	OR, SE (95% CI)			3.323, 0.321 (1.770, 6.237)
	Treatment P-value			0.00019
	Peto's OR (95% CI)			3.172 (1.752, 5.743)
	RR (95% CI)			2.304 (1.464, 3.625)
	Treatment P-value			0.00031
	RD (95% CI)			0.248 (0.125, 0.372)
	Treatment P-value			0.00008

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table ORC.BIN.S8.RES: Overall Response - Confirmed (Response Evaluable Set)
Subgroup: Primary Site of Tumor

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
Other	N, n (%)	190, 74 (38.9)	191, 33 (17.3)	
	OR, SE (95% CI)			3.054, 0.242 (1.899, 4.912)
	Treatment P-value			<.00001
	Interaction P-value [b]			0.83412
	Peto's OR (95% CI)			2.916 (1.866, 4.556)
	RR (95% CI)			2.254 (1.576, 3.224)
	Treatment P-value			<.00001
	Interaction P-value [b]			0.94139
	RD (95% CI)			0.217 (0.129, 0.304)
	Treatment P-value			<.00001
	Interaction P-value [b]			0.68321

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table ORC.BIN.S9.RES: Overall Response - Confirmed (Response Evaluable Set)
Subgroup: Prior Lines of Systemic Therapy

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
1-2 lines	N, n (%)	251, 103 (41.0)	262, 47 (17.9)	
	OR, SE (95% CI)			3.184, 0.206 (2.126, 4.766)
	Treatment P-value			<.00001
	Peto's OR (95% CI)			3.047 (2.083, 4.456)
	RR (95% CI)			2.288 (1.697, 3.083)
	Treatment P-value			<.00001
	RD (95% CI)			0.231 (0.154, 0.308)
	Treatment P-value			<.00001

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table ORC.BIN.S9.RES: Overall Response - Confirmed (Response Evaluable Set)
Subgroup: Prior Lines of Systemic Therapy

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
>=3 lines	N, n (%)	37, 14 (37.8)	34, 6 (17.6)	
	OR, SE (95% CI)			2.841, 0.563 (0.942, 8.568)
	Treatment P-value			0.06382
	Interaction P-value [b]			0.84976
	Peto's OR (95% CI)			2.675 (0.957, 7.475)
	RR (95% CI)			2.144 (0.930, 4.944)
	Treatment P-value			0.07352
	Interaction P-value [b]			0.88692
	RD (95% CI)			0.202 (-0.000, 0.404)
	Treatment P-value			0.05021
	Interaction P-value [b]			0.79159

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table ORC.BIN.S10.RES: Overall Response - Confirmed (Response Evaluable Set)
Subgroup: Best Response to Prior CPI

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
Responder	N, n (%)	56, 28 (50.0)	49, 12 (24.5)	
	OR, SE (95% CI)			3.083, 0.426 (1.337, 7.111)
	Treatment P-value			0.00827
	Peto's OR (95% CI)			2.920 (1.331, 6.406)
	RR (95% CI)			2.042 (1.170, 3.564)
	Treatment P-value			0.01203
	RD (95% CI)			0.255 (0.077, 0.433)
	Treatment P-value			0.00495

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table ORC.BIN.S10.RES: Overall Response - Confirmed (Response Evaluable Set)
Subgroup: Best Response to Prior CPI

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
Non-responder	N, n (%)	199, 79 (39.7)	207, 36 (17.4)	
	OR, SE (95% CI)			3.127, 0.234 (1.978, 4.944)
	Treatment P-value			<.00001
	Interaction P-value [b]			0.97689
	Peto's OR (95% CI)			2.992 (1.944, 4.606)
	RR (95% CI)			2.283 (1.620, 3.216)
	Treatment P-value			<.00001
	Interaction P-value [b]			0.74005
	RD (95% CI)			0.223 (0.138, 0.308)
	Treatment P-value			<.00001
	Interaction P-value [b]			0.75130

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

2.3.2 Krankheitskontrollrate

Astellas: 7465-CL-0301
Table DCC.BIN.S1.RES: Disease Control - Confirmed (Response Evaluable Set)
Subgroup: Age Group 1

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
<65 years	N, n (%)	104, 74 (71.2)	105, 47 (44.8)	
	OR, SE (95% CI)			3.044, 0.292 (1.717, 5.397)
	Treatment P-value			0.00014
	Peto's OR (95% CI)			2.937 (1.698, 5.080)
	RR (95% CI)			1.590 (1.244, 2.031)
	Treatment P-value			0.00021
	RD (95% CI)			0.264 (0.135, 0.393)
	Treatment P-value			0.00006

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DCC.BIN.S1.RES: Disease Control - Confirmed (Response Evaluable Set)
Subgroup: Age Group 1

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
>=65 years	N, n (%)	184, 133 (72.3)	191, 111 (58.1)	
	OR, SE (95% CI)			1.880, 0.221 (1.220, 2.896)
	Treatment P-value			0.00422
	Interaction P-value [b]			0.18637
	Peto's OR (95% CI)			1.862 (1.218, 2.845)
	RR (95% CI)			1.244 (1.071, 1.445)
	Treatment P-value			0.00437
	Interaction P-value [b]			0.08877
	RD (95% CI)			0.142 (0.046, 0.237)
	Treatment P-value			0.00356
	Interaction P-value [b]			0.13782

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DCC.BIN.S2.RES: Disease Control - Confirmed (Response Evaluable Set)
Subgroup: Age Group 2

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
<75 years	N, n (%)	237, 174 (73.4)	230, 117 (50.9)	
	OR, SE (95% CI)			2.667, 0.198 (1.811, 3.929)
	Treatment P-value			<.00001
	Peto's OR (95% CI)			2.607 (1.793, 3.789)
	RR (95% CI)			1.443 (1.244, 1.674)
	Treatment P-value			<.00001
	RD (95% CI)			0.225 (0.140, 0.311)
	Treatment P-value			<.00001

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DCC.BIN.S2.RES: Disease Control - Confirmed (Response Evaluable Set)
Subgroup: Age Group 2

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
>=75 years	N, n (%)	51, 33 (64.7)	66, 41 (62.1)	
	OR, SE (95% CI)			1.118, 0.388 (0.523, 2.390)
	Treatment P-value			0.77373
	Interaction P-value [b]			0.04702
	Peto's OR (95% CI)			1.117 (0.525, 2.375)
	RR (95% CI)			1.042 (0.790, 1.374)
	Treatment P-value			0.77279
	Interaction P-value [b]			0.04154
	RD (95% CI)			0.026 (-0.150, 0.202)
	Treatment P-value			0.77320
	Interaction P-value [b]			0.04297

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DCC.BIN.S3.RES: Disease Control - Confirmed (Response Evaluable Set)
Subgroup: Gender

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
Male	N, n (%)	228, 166 (72.8)	224, 120 (53.6)	
	OR, SE (95% CI)			2.320, 0.200 (1.567, 3.436)
	Treatment P-value			0.00003
	Peto's OR (95% CI)			2.284 (1.559, 3.347)
	RR (95% CI)			1.359 (1.175, 1.572)
	Treatment P-value			0.00004
	RD (95% CI)			0.192 (0.105, 0.280)
	Treatment P-value			0.00002

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DCC.BIN.S3.RES: Disease Control - Confirmed (Response Evaluable Set)
Subgroup: Gender

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
Female	N, n (%)	60, 41 (68.3)	72, 38 (52.8)	
	OR, SE (95% CI)			1.931, 0.364 (0.945, 3.943)
	Treatment P-value			0.07096
	Interaction P-value [b]			0.65897
	Peto's OR (95% CI)			1.901 (0.948, 3.814)
	RR (95% CI)			1.295 (0.980, 1.710)
	Treatment P-value			0.06881
	Interaction P-value [b]			0.76260
	RD (95% CI)			0.156 (-0.009, 0.320)
	Treatment P-value			0.06427
	Interaction P-value [b]			0.69801

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DCC.BIN.S4.RES: Disease Control - Confirmed (Response Evaluable Set)
Subgroup: Region

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
Western Europe	N, n (%)	117, 85 (72.6)	125, 67 (53.6)	
	OR, SE (95% CI)			2.299, 0.274 (1.343, 3.936)
	Treatment P-value			0.00239
	Peto's OR (95% CI)			2.253 (1.339, 3.791)
	RR (95% CI)			1.355 (1.113, 1.651)
	Treatment P-value			0.00253
	RD (95% CI)			0.190 (0.071, 0.310)
	Treatment P-value			0.00171

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DCC.BIN.S4.RES: Disease Control - Confirmed (Response Evaluable Set)
Subgroup: Region

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
US	N, n (%)	43, 26 (60.5)	41, 15 (36.6)	
	OR, SE (95% CI)			2.651, 0.450 (1.098, 6.403)
	Treatment P-value			0.03024
	Peto's OR (95% CI)			2.571 (1.098, 6.020)
	RR (95% CI)			1.653 (1.033, 2.644)
	Treatment P-value			0.03612
	RD (95% CI)			0.239 (0.031, 0.446)
	Treatment P-value			0.02416

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DCC.BIN.S4.RES: Disease Control - Confirmed (Response Evaluable Set)
Subgroup: Region

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
Rest of the World	N, n (%)	128, 96 (75.0)	130, 76 (58.5)	
	OR, SE (95% CI)			2.132, 0.271 (1.254, 3.624)
	Treatment P-value			0.00519
	Interaction P-value [b]			0.91603
	Peto's OR (95% CI)			2.099 (1.252, 3.519)
	RR (95% CI)			1.283 (1.076, 1.530)
	Treatment P-value			0.00555
	Interaction P-value [b]			0.59090
	RD (95% CI)			0.165 (0.052, 0.279)
	Treatment P-value			0.00417
	Interaction P-value [b]			0.82789

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DCC.BIN.S5.RES: Disease Control - Confirmed (Response Evaluable Set)
Subgroup: ECOG PS from IRT Strata

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
0	N, n (%)	115, 93 (80.9)	121, 76 (62.8)	
	OR, SE (95% CI)			2.503, 0.303 (1.383, 4.530)
	Treatment P-value			0.00243
	Peto's OR (95% CI)			2.422 (1.377, 4.261)
	RR (95% CI)			1.288 (1.093, 1.516)
	Treatment P-value			0.00243
	RD (95% CI)			0.181 (0.068, 0.293)
	Treatment P-value			0.00160

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DCC.BIN.S5.RES: Disease Control - Confirmed (Response Evaluable Set)
Subgroup: ECOG PS from IRT Strata

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
1	N, n (%)	173, 114 (65.9)	175, 82 (46.9)	
	OR, SE (95% CI)			2.191, 0.221 (1.422, 3.377)
	Treatment P-value			0.00038
	Interaction P-value [b]			0.72220
	Peto's OR (95% CI)			2.163 (1.417, 3.303)
	RR (95% CI)			1.406 (1.162, 1.702)
	Treatment P-value			0.00046
	Interaction P-value [b]			0.49116
	RD (95% CI)			0.190 (0.088, 0.293)
	Treatment P-value			0.00026
	Interaction P-value [b]			0.89939

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
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Astellas: 7465-CL-0301
Table DCC.BIN.S6.RES: Disease Control - Confirmed (Response Evaluable Set)
Subgroup: Liver Metastasis from IRT Strata

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
Yes	N, n (%)	93, 58 (62.4)	93, 38 (40.9)	
	OR, SE (95% CI)			2.398, 0.301 (1.331, 4.323)
	Treatment P-value			0.00360
	Peto's OR (95% CI)			2.355 (1.327, 4.179)
	RR (95% CI)			1.526 (1.141, 2.042)
	Treatment P-value			0.00441
	RD (95% CI)			0.215 (0.075, 0.355)
	Treatment P-value			0.00266

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DCC.BIN.S6.RES: Disease Control - Confirmed (Response Evaluable Set)
Subgroup: Liver Metastasis from IRT Strata

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
No	N, n (%)	195, 149 (76.4)	203, 120 (59.1)	
	OR, SE (95% CI)			2.240, 0.221 (1.453, 3.455)
	Treatment P-value			0.00026
	Interaction P-value [b]			0.85491
	Peto's OR (95% CI)			2.198 (1.445, 3.343)
	RR (95% CI)			1.293 (1.125, 1.485)
	Treatment P-value			0.00028
	Interaction P-value [b]			0.30637
	RD (95% CI)			0.173 (0.083, 0.263)
	Treatment P-value			0.00017
	Interaction P-value [b]			0.62173

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DCC.BIN.S7.RES: Disease Control - Confirmed (Response Evaluable Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
Paclitaxel	N, n (%)	134, 97 (72.4)	109, 60 (55.0)	
	OR, SE (95% CI)			2.141, 0.273 (1.254, 3.654)
	Treatment P-value			0.00526
	Peto's OR (95% CI)			2.128 (1.256, 3.607)
	RR (95% CI)			1.315 (1.077, 1.605)
	Treatment P-value			0.00707
	RD (95% CI)			0.173 (0.053, 0.294)
	Treatment P-value			0.00469

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DCC.BIN.S7.RES: Disease Control - Confirmed (Response Evaluable Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
Docetaxel	N, n (%)	84, 59 (70.2)	112, 51 (45.5)	
	OR, SE (95% CI)			2.823, 0.305 (1.553, 5.131)
	Treatment P-value			0.00066
	Peto's OR (95% CI)			2.713 (1.536, 4.791)
	RR (95% CI)			1.542 (1.206, 1.972)
	Treatment P-value			0.00055
	RD (95% CI)			0.247 (0.113, 0.381)
	Treatment P-value			0.00032

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DCC.BIN.S7.RES: Disease Control - Confirmed (Response Evaluable Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
Vinflunine	N, n (%)	70, 51 (72.9)	75, 47 (62.7)	
	OR, SE (95% CI)			1.599, 0.359 (0.790, 3.235)
	Treatment P-value			0.19160
	Interaction P-value [b]			0.48057
	Peto's OR (95% CI)			1.587 (0.793, 3.176)
	RR (95% CI)			1.163 (0.928, 1.457)
	Treatment P-value			0.19081
	Interaction P-value [b]			0.25243
	RD (95% CI)			0.102 (-0.049, 0.253)
	Treatment P-value			0.18626
	Interaction P-value [b]			0.37169

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DCC.BIN.S8.RES: Disease Control - Confirmed (Response Evaluable Set)
Subgroup: Primary Site of Tumor

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
Upper Tract	N, n (%)	98, 68 (69.4)	105, 57 (54.3)	
	OR, SE (95% CI)			1.909, 0.294 (1.073, 3.396)
	Treatment P-value			0.02787
	Peto's OR (95% CI)			1.887 (1.073, 3.319)
	RR (95% CI)			1.278 (1.026, 1.592)
	Treatment P-value			0.02828
	RD (95% CI)			0.151 (0.019, 0.283)
	Treatment P-value			0.02486

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DCC.BIN.S8.RES: Disease Control - Confirmed (Response Evaluable Set)
Subgroup: Primary Site of Tumor

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
Other	N, n (%)	190, 139 (73.2)	191, 101 (52.9)	
	OR, SE (95% CI)			2.429, 0.219 (1.582, 3.728)
	Treatment P-value			0.00005
	Interaction P-value [b]			0.51137
	Peto's OR (95% CI)			2.381 (1.572, 3.607)
	RR (95% CI)			1.383 (1.180, 1.622)
	Treatment P-value			0.00006
	Interaction P-value [b]			0.56804
	RD (95% CI)			0.203 (0.108, 0.298)
	Treatment P-value			0.00003
	Interaction P-value [b]			0.53152

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DCC.BIN.S9.RES: Disease Control - Confirmed (Response Evaluable Set)
Subgroup: Prior Lines of Systemic Therapy

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
1-2 lines	N, n (%)	251, 181 (72.1)	262, 139 (53.1)	
	OR, SE (95% CI)			2.288, 0.187 (1.585, 3.304)
	Treatment P-value			0.00001
	Peto's OR (95% CI)			2.249 (1.574, 3.214)
	RR (95% CI)			1.359 (1.185, 1.560)
	Treatment P-value			0.00001
	RD (95% CI)			0.191 (0.109, 0.273)
	Treatment P-value			<.00001

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DCC.BIN.S9.RES: Disease Control - Confirmed (Response Evaluable Set)
Subgroup: Prior Lines of Systemic Therapy

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
>=3 lines	N, n (%)	37, 26 (70.3)	34, 19 (55.9)	
	OR, SE (95% CI)			1.866, 0.499 (0.702, 4.959)
	Treatment P-value			0.21095
	Interaction P-value [b]			0.70255
	Peto's OR (95% CI)			1.843 (0.706, 4.811)
	RR (95% CI)			1.257 (0.873, 1.811)
	Treatment P-value			0.21844
	Interaction P-value [b]			0.69864
	RD (95% CI)			0.144 (-0.079, 0.366)
	Treatment P-value			0.20519
	Interaction P-value [b]			0.69877

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DCC.BIN.S10.RES: Disease Control - Confirmed (Response Evaluable Set)
Subgroup: Best Response to Prior CPI

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
Responder	N, n (%)	56, 49 (87.5)	49, 31 (63.3)	
	OR, SE (95% CI)			4.065, 0.501 (1.522, 10.852)
	Treatment P-value			0.00513
	Peto's OR (95% CI)			3.755 (1.533, 9.199)
	RR (95% CI)			1.383 (1.093, 1.750)
	Treatment P-value			0.00688
	RD (95% CI)			0.242 (0.082, 0.403)
	Treatment P-value			0.00306

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DCC.BIN.S10.RES: Disease Control - Confirmed (Response Evaluable Set)
Subgroup: Best Response to Prior CPI

Subgroup Level	Statistics	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy
Non-responder	N, n (%)	199, 137 (68.8)	207, 106 (51.2)	
	OR, SE (95% CI)			2.105, 0.207 (1.404, 3.158)
	Treatment P-value			0.00032
	Interaction P-value [b]			0.21580
	Peto's OR (95% CI)			2.080 (1.399, 3.091)
	RR (95% CI)			1.344 (1.143, 1.582)
	Treatment P-value			0.00036
	Interaction P-value [b]			0.84516
	RD (95% CI)			0.176 (0.083, 0.270)
	Treatment P-value			0.00022
	Interaction P-value [b]			0.48611

Analyses are based on a binomial regression model with logistic (OR), log (RR) and identity (RD) links. Peto's OR should be considered if there are 1% or 99% of events in any arm. Two-sided p-values are presented.
Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
[a] The Overall analysis is adjusted for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 13MAY2021 08:45
Analysis Plan: 15FEB2021 Confidential

2.3.3 Zeit bis zum Gesamtansprechen

Astellas: 7465-CL-0301
Table OR.KM.S1.RES: Time to Overall Response (Months) (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=15)
Overall	No. of Events (%)	42 (100.0)	15 (100.0)
	Median Survival Est. (95% CI)	1.86 (1.77, 1.94)	1.97 (1.84, 2.10)
	Hazard Ratio (95% CI)		1.225 (0.678, 2.214)
	Treatment P-value [a]		0.47280
	Interaction P-value [b]		0.48936

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table OR.KM.S1.RES: Time to Overall Response (Months) (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=75)	Chemotherapy (N=38)
Overall	No. of Events (%)	75 (100.0)	38 (100.0)
	Median Survival Est. (95% CI)	1.87 (1.81, 1.91)	1.91 (1.87, 2.04)
	Hazard Ratio (95% CI)		1.577 (1.059, 2.349)
	Treatment P-value [a]		0.02875
	Interaction P-value [b]		0.48936
6 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.03 (0.00, 0.12)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table OR.KM.S2.RES: Time to Overall Response (Months) (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=102)	Chemotherapy (N=38)
Overall	No. of Events (%)	102 (100.0)	38 (100.0)
	Median Survival Est. (95% CI)	1.87 (1.84, 1.91)	1.94 (1.87, 2.07)
	Hazard Ratio (95% CI)		1.451 (0.997, 2.112)
	Treatment P-value [a]		0.04063
	Interaction P-value [b]		0.96056

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table OR.KM.S2.RES: Time to Overall Response (Months) (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=15)	Chemotherapy (N=15)
Overall	No. of Events (%)	15 (100.0)	15 (100.0)
	Median Survival Est. (95% CI)	1.77 (1.68, 1.97)	1.91 (1.77, 2.07)
	Hazard Ratio (95% CI)		1.421 (0.685, 2.950)
	Treatment P-value [a]		0.27227
	Interaction P-value [b]		0.96056
6 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.07 (0.00, 0.26)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table OR.KM.S3.RES: Time to Overall Response (Months) (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=90)	Chemotherapy (N=37)
Overall	No. of Events (%)	90 (100.0)	37 (100.0)
	Median Survival Est. (95% CI)	1.87 (1.81, 1.91)	1.91 (1.87, 2.07)
	Hazard Ratio (95% CI)		1.621 (1.096, 2.398)
	Treatment P-value [a]		0.01825
	Interaction P-value [b]		0.29476
6 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.03 (0.00, 0.12)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table OR.KM.S3.RES: Time to Overall Response (Months) (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=27)	Chemotherapy (N=16)
Overall	No. of Events (%)	27 (100.0)	16 (100.0)
	Median Survival Est. (95% CI)	1.87 (1.77, 1.97)	1.95 (1.84, 2.04)
	Hazard Ratio (95% CI)		1.092 (0.586, 2.034)
	Treatment P-value [a]		0.86896
	Interaction P-value [b]		0.29476

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table OR.KM.S4.RES: Time to Overall Response (Months) (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=46)	Chemotherapy (N=22)
Overall	No. of Events (%)	46 (100.0)	22 (100.0)
	Median Survival Est. (95% CI)	1.84 (1.81, 1.91)	1.94 (1.87, 2.07)
	Hazard Ratio (95% CI)		1.660 (0.987, 2.791)
	Treatment P-value [a]		0.05925
	Interaction P-value [b]		0.68597
6 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.05 (0.00, 0.19)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table OR.KM.S4.RES: Time to Overall Response (Months) (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=15)	Chemotherapy (N=6)
Overall	No. of Events (%)	15 (100.0)	6 (100.0)
	Median Survival Est. (95% CI)	1.81 (1.68, 1.87)	1.89 (1.71, NC)
	Hazard Ratio (95% CI)		1.764 (0.678, 4.589)
	Treatment P-value [a]		0.40371
	Interaction P-value [b]		0.68597

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

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Table OR.KM.S4.RES: Time to Overall Response (Months) (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=56)	Chemotherapy (N=25)
Overall	No. of Events (%)	56 (100.0)	25 (100.0)
	Median Survival Est. (95% CI)	1.91 (1.77, 1.97)	1.91 (1.87, 2.07)
	Hazard Ratio (95% CI)		1.260 (0.784, 2.025)
	Treatment P-value [a]		0.14413
	Interaction P-value [b]		0.68597

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table OR.KM.S5.RES: Time to Overall Response (Months) (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=49)	Chemotherapy (N=30)
Overall	No. of Events (%)	49 (100.0)	30 (100.0)
	Median Survival Est. (95% CI)	1.84 (1.77, 1.94)	1.92 (1.87, 2.04)
	Hazard Ratio (95% CI)		1.333 (0.845, 2.103)
	Treatment P-value [a]		0.20005
	Interaction P-value [b]		0.56228

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

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Table OR.KM.S5.RES: Time to Overall Response (Months) (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=68)	Chemotherapy (N=23)
Overall	No. of Events (%)	68 (100.0)	23 (100.0)
	Median Survival Est. (95% CI)	1.87 (1.81, 1.91)	1.91 (1.81, 2.10)
	Hazard Ratio (95% CI)		1.623 (0.999, 2.639)
	Treatment P-value [a]		0.06091
	Interaction P-value [b]		0.56228
6 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.04 (0.00, 0.18)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

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Table OR.KM.S6.RES: Time to Overall Response (Months) (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=33)	Chemotherapy (N=10)
Overall	No. of Events (%)	33 (100.0)	10 (100.0)
	Median Survival Est. (95% CI)	1.84 (1.74, 1.91)	1.86 (1.45, 1.97)
	Hazard Ratio (95% CI)		0.733 (0.358, 1.501)
	Treatment P-value [a]		0.69473
	Interaction P-value [b]		0.05224

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

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Table OR.KM.S6.RES: Time to Overall Response (Months) (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=84)	Chemotherapy (N=43)
Overall	No. of Events (%)	84 (100.0)	43 (100.0)
	Median Survival Est. (95% CI)	1.87 (1.81, 1.94)	1.97 (1.91, 2.07)
	Hazard Ratio (95% CI)		1.645 (1.130, 2.396)
	Treatment P-value [a]		0.00725
	Interaction P-value [b]		0.05224
6 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.02 (0.00, 0.11)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table OR.KM.S7.RES: Time to Overall Response (Months) (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=56)	Chemotherapy (N=28)
Overall	No. of Events (%)	56 (100.0)	28 (100.0)
	Median Survival Est. (95% CI)	1.91 (1.84, 1.94)	1.91 (1.87, 2.00)
	Hazard Ratio (95% CI)		1.162 (0.732, 1.845)
	Treatment P-value [a]		0.54716
	Interaction P-value [b]		0.22833
6 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.04 (0.00, 0.15)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table OR.KM.S7.RES: Time to Overall Response (Months) (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=33)	Chemotherapy (N=13)
Overall	No. of Events (%)	33 (100.0)	13 (100.0)
	Median Survival Est. (95% CI)	1.81 (1.74, 1.87)	2.10 (1.87, 3.75)
	Hazard Ratio (95% CI)		2.320 (1.212, 4.443)
	Treatment P-value [a]		0.02186
	Interaction P-value [b]		0.22833

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table OR.KM.S7.RES: Time to Overall Response (Months) (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=28)	Chemotherapy (N=12)
Overall	No. of Events (%)	28 (100.0)	12 (100.0)
	Median Survival Est. (95% CI)	1.82 (1.71, 1.91)	1.91 (1.74, 2.14)
	Hazard Ratio (95% CI)		1.329 (0.674, 2.621)
	Treatment P-value [a]		0.41600
	Interaction P-value [b]		0.22833

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table OR.KM.S8.RES: Time to Overall Response (Months) (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=20)
Overall	No. of Events (%)	43 (100.0)	20 (100.0)
	Median Survival Est. (95% CI)	1.81 (1.74, 1.91)	1.95 (1.84, 2.17)
	Hazard Ratio (95% CI)		1.983 (1.159, 3.393)
	Treatment P-value [a]		0.00679
	Interaction P-value [b]		0.16494

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table OR.KM.S8.RES: Time to Overall Response (Months) (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=74)	Chemotherapy (N=33)
Overall	No. of Events (%)	74 (100.0)	33 (100.0)
	Median Survival Est. (95% CI)	1.89 (1.84, 1.94)	1.91 (1.87, 2.04)
	Hazard Ratio (95% CI)		1.226 (0.809, 1.858)
	Treatment P-value [a]		0.31794
	Interaction P-value [b]		0.16494
6 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.03 (0.00, 0.13)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table OR.KM.S9.RES: Time to Overall Response (Months) (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=103)	Chemotherapy (N=47)
Overall	No. of Events (%)	103 (100.0)	47 (100.0)
	Median Survival Est. (95% CI)	1.87 (1.81, 1.91)	1.94 (1.91, 2.07)
	Hazard Ratio (95% CI)		1.487 (1.048, 2.108)
	Treatment P-value [a]		0.02207
	Interaction P-value [b]		0.64913
6 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.02 (0.00, 0.10)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table OR.KM.S9.RES: Time to Overall Response (Months) (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=14)	Chemotherapy (N=6)
Overall	No. of Events (%)	14 (100.0)	6 (100.0)
	Median Survival Est. (95% CI)	1.84 (1.71, 1.97)	1.81 (1.64, NC)
	Hazard Ratio (95% CI)		1.173 (0.448, 3.068)
	Treatment P-value [a]		0.67093
	Interaction P-value [b]		0.64913

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table OR.KM.S10.RES: Time to Overall Response (Months) (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=28)	Chemotherapy (N=12)
Overall	No. of Events (%)	28 (100.0)	12 (100.0)
	Median Survival Est. (95% CI)	1.92 (1.81, 2.00)	1.91 (1.74, 2.07)
	Hazard Ratio (95% CI)		1.211 (0.615, 2.385)
	Treatment P-value [a]		0.44163
	Interaction P-value [b]		0.49701

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
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Astellas: 7465-CL-0301
Table OR.KM.S10.RES: Time to Overall Response (Months) (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=79)	Chemotherapy (N=36)
Overall	No. of Events (%)	79 (100.0)	36 (100.0)
	Median Survival Est. (95% CI)	1.87 (1.81, 1.91)	1.97 (1.87, 2.07)
	Hazard Ratio (95% CI)		1.590 (1.065, 2.373)
	Treatment P-value [a]		0.02839
	Interaction P-value [b]		0.49701
6 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.03 (0.00, 0.12)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

2.3.4 Dauer des Ansprechens

Astellas: 7465-CL-0301
Table DOR.KM.S1.RES: Duration of Response (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=15)
Overall	No. of Events (%)	24 (57.1)	7 (46.7)
	Median Survival Est. (95% CI)	5.65 (4.90, 9.46)	9.00 (5.59, NC)
	Hazard Ratio (95% CI)		1.562 (0.671, 3.634)
	Treatment P-value [a]		0.31325
	Interaction P-value [b]		0.18765
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.46 (0.29, 0.61)	9, 0.78 (0.47, 0.92)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.25 (0.10, 0.44)	0
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.25 (0.10, 0.44)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table DOR.KM.S1.RES: Duration of Response (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=75)	Chemotherapy (N=38)
Overall	No. of Events (%)	39 (52.0)	22 (57.9)
	Median Survival Est. (95% CI)	7.62 (5.59, 10.94)	5.98 (4.76, 10.09)
	Hazard Ratio (95% CI)		0.800 (0.474, 1.351)
	Treatment P-value [a]		0.39271
	Interaction P-value [b]		0.18765
6 Months	Patients at Risk, Survival Est. (95% CI)	31, 0.58 (0.46, 0.69)	13, 0.46 (0.28, 0.63)
12 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.30 (0.16, 0.44)	2, 0.21 (0.07, 0.40)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
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Astellas: 7465-CL-0301
Table DOR.KM.S2.RES: Duration of Response (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=102)	Chemotherapy (N=38)
Overall	No. of Events (%)	54 (52.9)	19 (50.0)
	Median Survival Est. (95% CI)	7.39 (5.52, 9.49)	9.00 (5.59, 10.09)
	Hazard Ratio (95% CI)		1.069 (0.633, 1.805)
	Treatment P-value [a]		0.80159
	Interaction P-value [b]		0.83389
6 Months	Patients at Risk, Survival Est. (95% CI)	40, 0.55 (0.44, 0.65)	17, 0.61 (0.42, 0.75)
12 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.30 (0.18, 0.42)	2, 0.23 (0.07, 0.46)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.30 (0.18, 0.42)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DOR.KM.S2.RES: Duration of Response (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=15)	Chemotherapy (N=15)
Overall	No. of Events (%)	9 (60.0)	10 (66.7)
	Median Survival Est. (95% CI)	5.59 (4.14, 9.23)	5.82 (3.71, 11.01)
	Hazard Ratio (95% CI)		0.956 (0.387, 2.360)
	Treatment P-value [a]		0.98133
	Interaction P-value [b]		0.83389
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.40 (0.13, 0.66)	5, 0.44 (0.17, 0.69)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DOR.KM.S3.RES: Duration of Response (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=90)	Chemotherapy (N=37)
Overall	No. of Events (%)	45 (50.0)	22 (59.5)
	Median Survival Est. (95% CI)	9.23 (5.59, 11.40)	7.59 (4.76, 9.00)
	Hazard Ratio (95% CI)		0.691 (0.414, 1.156)
	Treatment P-value [a]		0.18995
	Interaction P-value [b]		0.01165
6 Months	Patients at Risk, Survival Est. (95% CI)	35, 0.55 (0.44, 0.66)	14, 0.51 (0.33, 0.67)
12 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.34 (0.21, 0.48)	1, 0.17 (0.04, 0.39)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.34 (0.21, 0.48)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DOR.KM.S3.RES: Duration of Response (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=27)	Chemotherapy (N=16)
Overall	No. of Events (%)	18 (66.7)	7 (43.8)
	Median Survival Est. (95% CI)	5.95 (3.75, 7.69)	9.56 (5.82, NC)
	Hazard Ratio (95% CI)		2.591 (1.074, 6.250)
	Treatment P-value [a]		0.00725
	Interaction P-value [b]		0.01165
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.49 (0.28, 0.68)	8, 0.68 (0.35, 0.87)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.27 (0.04, 0.58)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DOR.KM.S4.RES: Duration of Response (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=46)	Chemotherapy (N=22)
Overall	No. of Events (%)	25 (54.3)	10 (45.5)
	Median Survival Est. (95% CI)	7.16 (5.52, NC)	9.00 (5.68, NC)
	Hazard Ratio (95% CI)		1.370 (0.657, 2.857)
	Treatment P-value [a]		0.38383
	Interaction P-value [b]		0.38730
6 Months	Patients at Risk, Survival Est. (95% CI)	18, 0.55 (0.39, 0.69)	13, 0.69 (0.44, 0.85)
12 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.32 (0.16, 0.50)	1, 0.36 (0.11, 0.61)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DOR.KM.S4.RES: Duration of Response (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=15)	Chemotherapy (N=6)
Overall	No. of Events (%)	8 (53.3)	6 (100.0)
	Median Survival Est. (95% CI)	10.94 (4.14, NC)	8.77 (5.65, NC)
	Hazard Ratio (95% CI)		0.593 (0.205, 1.716)
	Treatment P-value [a]		0.28529
	Interaction P-value [b]		0.38730
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.60 (0.32, 0.80)	4, 0.67 (0.19, 0.90)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.41 (0.15, 0.66)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DOR.KM.S4.RES: Duration of Response (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=56)	Chemotherapy (N=25)
Overall	No. of Events (%)	30 (53.6)	13 (52.0)
	Median Survival Est. (95% CI)	7.46 (4.07, 9.46)	5.59 (3.78, NC)
	Hazard Ratio (95% CI)		0.818 (0.425, 1.576)
	Treatment P-value [a]		0.66428
	Interaction P-value [b]		0.38730
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.50 (0.35, 0.64)	5, 0.40 (0.18, 0.61)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.19 (0.06, 0.37)	1, 0.26 (0.06, 0.53)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.19 (0.06, 0.37)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DOR.KM.S5.RES: Duration of Response (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=49)	Chemotherapy (N=30)
Overall	No. of Events (%)	22 (44.9)	14 (46.7)
	Median Survival Est. (95% CI)	9.46 (5.68, NC)	9.56 (5.59, 11.01)
	Hazard Ratio (95% CI)		0.862 (0.441, 1.687)
	Treatment P-value [a]		0.62261
	Interaction P-value [b]		0.74766
6 Months	Patients at Risk, Survival Est. (95% CI)	22, 0.65 (0.48, 0.77)	14, 0.65 (0.43, 0.81)
12 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.33 (0.15, 0.52)	1, 0.21 (0.04, 0.47)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.33 (0.15, 0.52)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

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Table DOR.KM.S5.RES: Duration of Response (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=68)	Chemotherapy (N=23)
Overall	No. of Events (%)	41 (60.3)	15 (65.2)
	Median Survival Est. (95% CI)	5.65 (5.26, 7.69)	5.98 (4.04, 9.00)
	Hazard Ratio (95% CI)		0.999 (0.552, 1.806)
	Treatment P-value [a]		0.99160
	Interaction P-value [b]		0.74766
6 Months	Patients at Risk, Survival Est. (95% CI)	22, 0.46 (0.33, 0.58)	8, 0.45 (0.22, 0.65)
12 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.25 (0.13, 0.39)	1, 0.16 (0.03, 0.38)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DOR.KM.S6.RES: Duration of Response (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=33)	Chemotherapy (N=10)
Overall	No. of Events (%)	21 (63.6)	4 (40.0)
	Median Survival Est. (95% CI)	7.16 (5.29, 9.13)	11.01 (3.71, NC)
	Hazard Ratio (95% CI)		2.028 (0.693, 5.934)
	Treatment P-value [a]		0.14071
	Interaction P-value [b]		0.12081
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.50 (0.31, 0.66)	3, 0.54 (0.13, 0.83)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.09 (0.01, 0.31)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table DOR.KM.S6.RES: Duration of Response (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=84)	Chemotherapy (N=43)
Overall	No. of Events (%)	42 (50.0)	25 (58.1)
	Median Survival Est. (95% CI)	7.69 (5.59, 11.40)	8.11 (5.16, 9.43)
	Hazard Ratio (95% CI)		0.793 (0.482, 1.304)
	Treatment P-value [a]		0.38605
	Interaction P-value [b]		0.12081
6 Months	Patients at Risk, Survival Est. (95% CI)	33, 0.55 (0.43, 0.66)	19, 0.55 (0.38, 0.70)
12 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.33 (0.20, 0.47)	2, 0.17 (0.05, 0.36)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.33 (0.20, 0.47)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table DOR.KM.S7.RES: Duration of Response (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=56)	Chemotherapy (N=28)
Overall	No. of Events (%)	31 (55.4)	16 (57.1)
	Median Survival Est. (95% CI)	6.44 (5.52, 9.46)	5.98 (4.76, 8.25)
	Hazard Ratio (95% CI)		0.885 (0.482, 1.623)
	Treatment P-value [a]		0.82320
	Interaction P-value [b]		0.31480
6 Months	Patients at Risk, Survival Est. (95% CI)	20, 0.51 (0.36, 0.64)	10, 0.48 (0.27, 0.67)
12 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.29 (0.15, 0.44)	1, 0.14 (0.01, 0.41)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.29 (0.15, 0.44)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
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Astellas: 7465-CL-0301
Table DOR.KM.S7.RES: Duration of Response (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=33)	Chemotherapy (N=13)
Overall	No. of Events (%)	18 (54.5)	9 (69.2)
	Median Survival Est. (95% CI)	9.23 (4.86, 11.40)	8.11 (3.68, NC)
	Hazard Ratio (95% CI)		0.703 (0.315, 1.569)
	Treatment P-value [a]		0.39280
	Interaction P-value [b]		0.31480
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.54 (0.34, 0.70)	5, 0.53 (0.23, 0.75)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.28 (0.09, 0.50)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DOR.KM.S7.RES: Duration of Response (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=28)	Chemotherapy (N=12)
Overall	No. of Events (%)	14 (50.0)	4 (33.3)
	Median Survival Est. (95% CI)	7.39 (4.90, NC)	11.01 (3.68, NC)
	Hazard Ratio (95% CI)		2.010 (0.659, 6.131)
	Treatment P-value [a]		0.23904
	Interaction P-value [b]		0.31480
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.59 (0.37, 0.76)	7, 0.79 (0.38, 0.94)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.27 (0.06, 0.54)	1, 0.47 (0.12, 0.77)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DOR.KM.S8.RES: Duration of Response (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=20)
Overall	No. of Events (%)	22 (51.2)	8 (40.0)
	Median Survival Est. (95% CI)	9.13 (5.52, 11.40)	10.09 (5.16, NC)
	Hazard Ratio (95% CI)		1.489 (0.662, 3.346)
	Treatment P-value [a]		0.32856
	Interaction P-value [b]		0.18258
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.58 (0.41, 0.72)	10, 0.70 (0.42, 0.86)
12 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.31 (0.14, 0.50)	2, 0.41 (0.15, 0.67)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.31 (0.14, 0.50)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table DOR.KM.S8.RES: Duration of Response (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=74)	Chemotherapy (N=33)
Overall	No. of Events (%)	41 (55.4)	21 (63.6)
	Median Survival Est. (95% CI)	6.44 (5.52, 9.46)	5.98 (4.04, 8.25)
	Hazard Ratio (95% CI)		0.771 (0.454, 1.308)
	Treatment P-value [a]		0.32827
	Interaction P-value [b]		0.18258
6 Months	Patients at Risk, Survival Est. (95% CI)	27, 0.51 (0.39, 0.63)	12, 0.48 (0.28, 0.65)
12 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.27 (0.14, 0.41)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DOR.KM.S9.RES: Duration of Response (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=103)	Chemotherapy (N=47)
Overall	No. of Events (%)	55 (53.4)	26 (55.3)
	Median Survival Est. (95% CI)	7.46 (5.59, 9.46)	8.11 (5.65, 9.56)
	Hazard Ratio (95% CI)		0.949 (0.595, 1.514)
	Treatment P-value [a]		0.81178
	Interaction P-value [b]		0.65639
6 Months	Patients at Risk, Survival Est. (95% CI)	40, 0.55 (0.44, 0.64)	20, 0.56 (0.40, 0.70)
12 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.31 (0.20, 0.43)	1, 0.18 (0.05, 0.37)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.31 (0.20, 0.43)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DOR.KM.S9.RES: Duration of Response (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=14)	Chemotherapy (N=6)
Overall	No. of Events (%)	8 (57.1)	3 (50.0)
	Median Survival Est. (95% CI)	5.95 (3.52, NC)	8.21 (3.52, NC)
	Hazard Ratio (95% CI)		1.306 (0.346, 4.933)
	Treatment P-value [a]		0.57183
	Interaction P-value [b]		0.65639
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.46 (0.16, 0.72)	2, 0.56 (0.07, 0.88)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.28 (0.01, 0.70)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DOR.KM.S10.RES: Duration of Response (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=28)	Chemotherapy (N=12)
Overall	No. of Events (%)	12 (42.9)	8 (66.7)
	Median Survival Est. (95% CI)	9.49 (5.26, NC)	5.82 (3.68, 8.21)
	Hazard Ratio (95% CI)		0.538 (0.220, 1.318)
	Treatment P-value [a]		0.18553
	Interaction P-value [b]		0.14706
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.61 (0.38, 0.78)	5, 0.46 (0.17, 0.71)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.30 (0.06, 0.58)	1, 0.15 (0.01, 0.47)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DOR.KM.S10.RES: Duration of Response (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=79)	Chemotherapy (N=36)
Overall	No. of Events (%)	46 (58.2)	19 (52.8)
	Median Survival Est. (95% CI)	6.44 (5.49, 9.23)	8.25 (5.59, 10.09)
	Hazard Ratio (95% CI)		1.164 (0.682, 1.988)
	Treatment P-value [a]		0.59761
	Interaction P-value [b]		0.14706
6 Months	Patients at Risk, Survival Est. (95% CI)	28, 0.51 (0.38, 0.62)	14, 0.55 (0.35, 0.72)
12 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.25 (0.14, 0.38)	1, 0.20 (0.05, 0.41)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.25 (0.14, 0.38)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

2.3.5 Zeit bis zur Krankheitskontrolle

Astellas: 7465-CL-0301
Table DC.KM.S1.RES: Time to Disease Control (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response or Stable Disease)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=74)	Chemotherapy (N=47)
Overall	No. of Events (%)	74 (100.0)	47 (100.0)
	Median Survival Est. (95% CI)	1.87 (1.81, 1.91)	1.91 (1.91, 1.97)
	Hazard Ratio (95% CI)		1.053 (0.728, 1.523)
	Treatment P-value [a]		0.83739
	Interaction P-value [b]		0.39789

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DC.KM.S1.RES: Time to Disease Control (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response or Stable Disease)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=133)	Chemotherapy (N=111)
Overall	No. of Events (%)	133 (100.0)	111 (100.0)
	Median Survival Est. (95% CI)	1.91 (1.84, 1.91)	1.94 (1.91, 2.00)
	Hazard Ratio (95% CI)		1.277 (0.992, 1.645)
	Treatment P-value [a]		0.04925
	Interaction P-value [b]		0.39789
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.01 (0.00, 0.04)	1, 0.01 (0.00, 0.04)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DC.KM.S2.RES: Time to Disease Control (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response or Stable Disease)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=174)	Chemotherapy (N=117)
Overall	No. of Events (%)	174 (100.0)	117 (100.0)
	Median Survival Est. (95% CI)	1.91 (1.87, 1.91)	1.94 (1.91, 1.97)
	Hazard Ratio (95% CI)		1.179 (0.931, 1.492)
	Treatment P-value [a]		0.16441
	Interaction P-value [b]		0.56135
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.01 (0.00, 0.03)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DC.KM.S2.RES: Time to Disease Control (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response or Stable Disease)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=33)	Chemotherapy (N=41)
Overall	No. of Events (%)	33 (100.0)	41 (100.0)
	Median Survival Est. (95% CI)	1.84 (1.74, 1.87)	1.91 (1.87, 2.00)
	Hazard Ratio (95% CI)		1.374 (0.867, 2.176)
	Treatment P-value [a]		0.12332
	Interaction P-value [b]		0.56135
6 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.02 (0.00, 0.11)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DC.KM.S3.RES: Time to Disease Control (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response or Stable Disease)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=166)	Chemotherapy (N=120)
Overall	No. of Events (%)	166 (100.0)	120 (100.0)
	Median Survival Est. (95% CI)	1.87 (1.84, 1.91)	1.91 (1.91, 1.97)
	Hazard Ratio (95% CI)		1.231 (0.972, 1.558)
	Treatment P-value [a]		0.07986
	Interaction P-value [b]		0.66785
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.01 (0.00, 0.03)	1, 0.01 (0.00, 0.04)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
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Astellas: 7465-CL-0301
Table DC.KM.S3.RES: Time to Disease Control (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response or Stable Disease)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=41)	Chemotherapy (N=38)
Overall	No. of Events (%)	41 (100.0)	38 (100.0)
	Median Survival Est. (95% CI)	1.91 (1.81, 1.97)	1.94 (1.91, 1.97)
	Hazard Ratio (95% CI)		1.103 (0.709, 1.716)
	Treatment P-value [a]		0.70634
	Interaction P-value [b]		0.66785

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table DC.KM.S4.RES: Time to Disease Control (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response or Stable Disease)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=67)
Overall	No. of Events (%)	85 (100.0)	67 (100.0)
	Median Survival Est. (95% CI)	1.87 (1.84, 1.91)	1.94 (1.91, 2.04)
	Hazard Ratio (95% CI)		1.434 (1.039, 1.978)
	Treatment P-value [a]		0.02075
	Interaction P-value [b]		0.17205
6 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.01 (0.00, 0.07)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
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Astellas: 7465-CL-0301
Table DC.KM.S4.RES: Time to Disease Control (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response or Stable Disease)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=26)	Chemotherapy (N=15)
Overall	No. of Events (%)	26 (100.0)	15 (100.0)
	Median Survival Est. (95% CI)	1.81 (1.74, 1.87)	2.00 (1.77, 2.07)
	Hazard Ratio (95% CI)		1.555 (0.820, 2.948)
	Treatment P-value [a]		0.23203
	Interaction P-value [b]		0.17205

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DC.KM.S4.RES: Time to Disease Control (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response or Stable Disease)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=76)
Overall	No. of Events (%)	96 (100.0)	76 (100.0)
	Median Survival Est. (95% CI)	1.91 (1.87, 1.94)	1.91 (1.87, 1.97)
	Hazard Ratio (95% CI)		0.979 (0.723, 1.326)
	Treatment P-value [a]		0.94546
	Interaction P-value [b]		0.17205
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.01 (0.00, 0.05)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DC.KM.S5.RES: Time to Disease Control (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response or Stable Disease)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=76)
Overall	No. of Events (%)	93 (100.0)	76 (100.0)
	Median Survival Est. (95% CI)	1.91 (1.84, 1.94)	1.92 (1.91, 1.97)
	Hazard Ratio (95% CI)		1.137 (0.839, 1.541)
	Treatment P-value [a]		0.40864
	Interaction P-value [b]		0.62999

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DC.KM.S5.RES: Time to Disease Control (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response or Stable Disease)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=114)	Chemotherapy (N=82)
Overall	No. of Events (%)	114 (100.0)	82 (100.0)
	Median Survival Est. (95% CI)	1.87 (1.84, 1.91)	1.92 (1.91, 2.00)
	Hazard Ratio (95% CI)		1.260 (0.947, 1.676)
	Treatment P-value [a]		0.09188
	Interaction P-value [b]		0.62999
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.01 (0.00, 0.04)	1, 0.01 (0.00, 0.06)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DC.KM.S6.RES: Time to Disease Control (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response or Stable Disease)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=58)	Chemotherapy (N=38)
Overall	No. of Events (%)	58 (100.0)	38 (100.0)
	Median Survival Est. (95% CI)	1.86 (1.81, 1.91)	1.92 (1.87, 2.00)
	Hazard Ratio (95% CI)		1.234 (0.818, 1.862)
	Treatment P-value [a]		0.28931
	Interaction P-value [b]		0.86417

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DC.KM.S6.RES: Time to Disease Control (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response or Stable Disease)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=149)	Chemotherapy (N=120)
Overall	No. of Events (%)	149 (100.0)	120 (100.0)
	Median Survival Est. (95% CI)	1.91 (1.87, 1.91)	1.92 (1.91, 1.97)
	Hazard Ratio (95% CI)		1.184 (0.930, 1.507)
	Treatment P-value [a]		0.13803
	Interaction P-value [b]		0.86417
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.01 (0.00, 0.03)	1, 0.01 (0.00, 0.04)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

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Table DC.KM.S7.RES: Time to Disease Control (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response or Stable Disease)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=97)	Chemotherapy (N=60)
Overall	No. of Events (%)	97 (100.0)	60 (100.0)
	Median Survival Est. (95% CI)	1.91 (1.87, 1.94)	1.91 (1.91, 1.97)
	Hazard Ratio (95% CI)		0.964 (0.697, 1.333)
	Treatment P-value [a]		0.98322
	Interaction P-value [b]		0.13231
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.01 (0.00, 0.05)	1, 0.02 (0.00, 0.08)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
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Astellas: 7465-CL-0301
Table DC.KM.S7.RES: Time to Disease Control (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response or Stable Disease)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=59)	Chemotherapy (N=51)
Overall	No. of Events (%)	59 (100.0)	51 (100.0)
	Median Survival Est. (95% CI)	1.87 (1.81, 1.91)	1.97 (1.91, 2.00)
	Hazard Ratio (95% CI)		1.497 (1.028, 2.180)
	Treatment P-value [a]		0.03826
	Interaction P-value [b]		0.13231

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DC.KM.S7.RES: Time to Disease Control (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response or Stable Disease)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=47)
Overall	No. of Events (%)	51 (100.0)	47 (100.0)
	Median Survival Est. (95% CI)	1.84 (1.74, 1.91)	1.91 (1.87, 2.00)
	Hazard Ratio (95% CI)		1.482 (0.996, 2.207)
	Treatment P-value [a]		0.07506
	Interaction P-value [b]		0.13231

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DC.KM.S8.RES: Time to Disease Control (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response or Stable Disease)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=68)	Chemotherapy (N=57)
Overall	No. of Events (%)	68 (100.0)	57 (100.0)
	Median Survival Est. (95% CI)	1.82 (1.74, 1.91)	1.94 (1.91, 2.00)
	Hazard Ratio (95% CI)		1.425 (1.000, 2.031)
	Treatment P-value [a]		0.05902
	Interaction P-value [b]		0.24521
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.01 (0.00, 0.07)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DC.KM.S8.RES: Time to Disease Control (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response or Stable Disease)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=139)	Chemotherapy (N=101)
Overall	No. of Events (%)	139 (100.0)	101 (100.0)
	Median Survival Est. (95% CI)	1.91 (1.87, 1.91)	1.91 (1.91, 1.97)
	Hazard Ratio (95% CI)		1.099 (0.850, 1.422)
	Treatment P-value [a]		0.43188
	Interaction P-value [b]		0.24521
6 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.01 (0.00, 0.05)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

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Table DC.KM.S9.RES: Time to Disease Control (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response or Stable Disease)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=139)
Overall	No. of Events (%)	181 (100.0)	139 (100.0)
	Median Survival Est. (95% CI)	1.87 (1.84, 1.91)	1.94 (1.91, 1.97)
	Hazard Ratio (95% CI)		1.179 (0.944, 1.473)
	Treatment P-value [a]		0.10971
	Interaction P-value [b]		0.62687
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.01 (0.00, 0.03)	1, 0.01 (0.00, 0.04)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DC.KM.S9.RES: Time to Disease Control (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response or Stable Disease)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=26)	Chemotherapy (N=19)
Overall	No. of Events (%)	26 (100.0)	19 (100.0)
	Median Survival Est. (95% CI)	1.89 (1.77, 1.94)	1.91 (1.74, 2.04)
	Hazard Ratio (95% CI)		1.380 (0.763, 2.496)
	Treatment P-value [a]		0.22586
	Interaction P-value [b]		0.62687

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

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Table DC.KM.S10.RES: Time to Disease Control (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response or Stable Disease)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=49)	Chemotherapy (N=31)
Overall	No. of Events (%)	49 (100.0)	31 (100.0)
	Median Survival Est. (95% CI)	1.91 (1.84, 1.94)	1.91 (1.87, 2.00)
	Hazard Ratio (95% CI)		1.030 (0.655, 1.620)
	Treatment P-value [a]		0.71454
	Interaction P-value [b]		0.48314
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.02 (0.00, 0.09)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 16APR2021 11:47
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table DC.KM.S10.RES: Time to Disease Control (Months) - Confirmed (Response Evaluable Set - Patients with Confirmed Complete Response or Confirmed Partial Response or Stable Disease)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=137)	Chemotherapy (N=106)
Overall	No. of Events (%)	137 (100.0)	106 (100.0)
	Median Survival Est. (95% CI)	1.87 (1.84, 1.91)	1.94 (1.91, 1.97)
	Hazard Ratio (95% CI)		1.241 (0.962, 1.600)
	Treatment P-value [a]		0.09398
	Interaction P-value [b]		0.48314
6 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.01 (0.00, 0.05)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of > 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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2.4 Subgruppenanalysen zur Symptomatik anhand des EORTC QLQ-C30

2.4.1 Primäranalyse (MID ≥ 10 Punkte)

2.4.1.1 Fatigue

Astellas: 7465-CL-0301
Table EORTC10.FS.KM.S1.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	71 (65.7)	58 (52.3)
	Median Survival Est. (95% CI)	0.76 (0.56, 0.95)	0.76 (0.53, 1.48)
	Hazard Ratio (95% CI)		0.998 (0.706, 1.413)
	Treatment P-value [a]		0.93785
	Interaction P-value [b]		0.40163
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.21 (0.12, 0.32)	5, 0.19 (0.10, 0.31)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.FS.KM.S1.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	126 (65.3)	122 (62.2)
	Median Survival Est. (95% CI)	0.76 (0.56, 0.99)	0.62 (0.39, 0.79)
	Hazard Ratio (95% CI)		0.832 (0.648, 1.067)
	Treatment P-value [a]		0.17665
	Interaction P-value [b]		0.40163
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.19 (0.13, 0.27)	5, 0.11 (0.06, 0.18)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.10 (0.03, 0.22)	1, 0.07 (0.02, 0.17)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.FS.KM.S2.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	162 (65.1)	136 (56.9)
	Median Survival Est. (95% CI)	0.79 (0.59, 0.99)	0.72 (0.43, 0.79)
	Hazard Ratio (95% CI)		0.828 (0.659, 1.041)
	Treatment P-value [a]		0.09155
	Interaction P-value [b]		0.08525
6 Months	Patients at Risk, Survival Est. (95% CI)	18, 0.22 (0.16, 0.29)	7, 0.14 (0.09, 0.22)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.06 (0.01, 0.19)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.FS.KM.S2.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	35 (67.3)	44 (64.7)
	Median Survival Est. (95% CI)	0.53 (0.33, 0.69)	0.79 (0.43, 0.99)
	Hazard Ratio (95% CI)		1.285 (0.824, 2.004)
	Treatment P-value [a]		0.22702
	Interaction P-value [b]		0.08525
6 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.08 (0.02, 0.21)	3, 0.12 (0.05, 0.23)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.08 (0.02, 0.21)	1, 0.12 (0.05, 0.23)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.FS.KM.S3.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	159 (66.8)	135 (58.2)
	Median Survival Est. (95% CI)	0.76 (0.59, 0.95)	0.72 (0.43, 0.79)
	Hazard Ratio (95% CI)		0.900 (0.715, 1.133)
	Treatment P-value [a]		0.38588
	Interaction P-value [b]		0.73254
6 Months	Patients at Risk, Survival Est. (95% CI)	19, 0.20 (0.14, 0.27)	8, 0.15 (0.10, 0.22)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.08 (0.02, 0.17)	1, 0.07 (0.02, 0.17)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.FS.KM.S3.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	38 (60.3)	45 (60.0)
	Median Survival Est. (95% CI)	0.69 (0.49, 1.45)	0.79 (0.36, 0.99)
	Hazard Ratio (95% CI)		0.827 (0.537, 1.273)
	Treatment P-value [a]		0.32971
	Interaction P-value [b]		0.73254
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.18 (0.07, 0.34)	2, 0.10 (0.02, 0.23)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.FS.KM.S4.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	72 (57.1)	63 (48.8)
	Median Survival Est. (95% CI)	0.79 (0.56, 1.05)	0.56 (0.36, 0.79)
	Hazard Ratio (95% CI)		0.811 (0.578, 1.138)
	Treatment P-value [a]		0.25400
	Interaction P-value [b]		0.72150
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.21 (0.12, 0.33)	5, 0.19 (0.11, 0.29)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.FS.KM.S4.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	26 (60.5)	21 (47.7)
	Median Survival Est. (95% CI)	0.82 (0.36, 1.48)	0.79 (0.53, 1.71)
	Hazard Ratio (95% CI)		1.059 (0.595, 1.886)
	Treatment P-value [a]		0.83021
	Interaction P-value [b]		0.72150
6 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.13 (0.04, 0.29)	1, 0.12 (0.01, 0.37)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.07 (0.01, 0.24)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Table EORTC10.FS.KM.S4.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	99 (75.0)	96 (71.6)
	Median Survival Est. (95% CI)	0.62 (0.53, 0.82)	0.76 (0.43, 1.02)
	Hazard Ratio (95% CI)		0.906 (0.684, 1.201)
	Treatment P-value [a]		0.42528
	Interaction P-value [b]		0.72150
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.20 (0.13, 0.29)	4, 0.11 (0.05, 0.19)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.09 (0.04, 0.19)	1, 0.05 (0.01, 0.14)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.FS.KM.S5.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	86 (71.7)	84 (67.7)
	Median Survival Est. (95% CI)	0.79 (0.59, 0.99)	0.72 (0.36, 0.82)
	Hazard Ratio (95% CI)		0.787 (0.582, 1.065)
	Treatment P-value [a]		0.07300
	Interaction P-value [b]		0.30402
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.17 (0.10, 0.27)	2, 0.09 (0.03, 0.21)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.09 (0.03, 0.18)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Table EORTC10.FS.KM.S5.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	111 (61.3)	96 (52.5)
	Median Survival Est. (95% CI)	0.62 (0.53, 0.82)	0.76 (0.49, 0.99)
	Hazard Ratio (95% CI)		0.975 (0.742, 1.281)
	Treatment P-value [a]		0.86472
	Interaction P-value [b]		0.30402
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.22 (0.15, 0.29)	8, 0.16 (0.10, 0.24)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.08 (0.01, 0.24)	1, 0.10 (0.03, 0.21)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Table EORTC10.FS.KM.S6.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	58 (62.4)	49 (51.6)
	Median Survival Est. (95% CI)	0.56 (0.36, 0.92)	0.53 (0.36, 0.82)
	Hazard Ratio (95% CI)		0.842 (0.575, 1.234)
	Treatment P-value [a]		0.47811
	Interaction P-value [b]		0.78334
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.20 (0.11, 0.31)	1, 0.14 (0.06, 0.25)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.14 (0.05, 0.25)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Table EORTC10.FS.KM.S6.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	139 (66.8)	131 (61.8)
	Median Survival Est. (95% CI)	0.79 (0.59, 0.99)	0.76 (0.53, 0.95)
	Hazard Ratio (95% CI)		0.897 (0.707, 1.140)
	Treatment P-value [a]		0.39016
	Interaction P-value [b]		0.78334
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.20 (0.13, 0.27)	9, 0.15 (0.09, 0.22)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.06 (0.01, 0.18)	1, 0.07 (0.02, 0.17)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.FS.KM.S7.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	94 (66.7)	66 (58.9)
	Median Survival Est. (95% CI)	0.72 (0.53, 0.99)	0.76 (0.43, 1.08)
	Hazard Ratio (95% CI)		0.879 (0.641, 1.205)
	Treatment P-value [a]		0.41102
	Interaction P-value [b]		0.99344
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.22 (0.15, 0.31)	3, 0.12 (0.05, 0.21)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.14 (0.07, 0.23)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Table EORTC10.FS.KM.S7.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	60 (69.0)	70 (59.8)
	Median Survival Est. (95% CI)	0.62 (0.53, 0.82)	0.59 (0.33, 0.82)
	Hazard Ratio (95% CI)		0.899 (0.637, 1.270)
	Treatment P-value [a]		0.54726
	Interaction P-value [b]		0.99344
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.15 (0.07, 0.26)	3, 0.13 (0.05, 0.25)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.04 (0.00, 0.15)	1, 0.09 (0.02, 0.21)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.FS.KM.S7.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	43 (58.9)	44 (56.4)
	Median Survival Est. (95% CI)	0.85 (0.53, 1.28)	0.72 (0.43, 0.99)
	Hazard Ratio (95% CI)		0.901 (0.592, 1.372)
	Treatment P-value [a]		0.59786
	Interaction P-value [b]		0.99344
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.20 (0.08, 0.35)	4, 0.18 (0.08, 0.30)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.FS.KM.S8.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	63 (64.3)	76 (71.0)
	Median Survival Est. (95% CI)	0.62 (0.56, 0.99)	0.56 (0.36, 0.79)
	Hazard Ratio (95% CI)		0.746 (0.534, 1.043)
	Treatment P-value [a]		0.08833
	Interaction P-value [b]		0.19095
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.23 (0.14, 0.33)	3, 0.08 (0.03, 0.17)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.12 (0.04, 0.23)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.FS.KM.S8.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	134 (66.0)	104 (52.0)
	Median Survival Est. (95% CI)	0.76 (0.56, 0.95)	0.76 (0.53, 1.05)
	Hazard Ratio (95% CI)		0.988 (0.765, 1.277)
	Treatment P-value [a]		0.90172
	Interaction P-value [b]		0.19095
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.18 (0.12, 0.26)	7, 0.18 (0.11, 0.26)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.06 (0.01, 0.20)	1, 0.08 (0.01, 0.23)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.FS.KM.S9.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	169 (64.5)	158 (58.5)
	Median Survival Est. (95% CI)	0.76 (0.59, 0.95)	0.72 (0.49, 0.82)
	Hazard Ratio (95% CI)		0.842 (0.677, 1.046)
	Treatment P-value [a]		0.11047
	Interaction P-value [b]		0.21887
6 Months	Patients at Risk, Survival Est. (95% CI)	18, 0.21 (0.15, 0.28)	8, 0.13 (0.08, 0.19)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.09 (0.03, 0.19)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.FS.KM.S9.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	28 (71.8)	22 (59.5)
	Median Survival Est. (95% CI)	0.69 (0.39, 1.08)	0.76 (0.33, 1.74)
	Hazard Ratio (95% CI)		1.228 (0.701, 2.151)
	Treatment P-value [a]		0.49351
	Interaction P-value [b]		0.21887
6 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.12 (0.02, 0.29)	2, 0.18 (0.05, 0.39)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.18 (0.05, 0.39)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.FS.KM.S10.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	44 (72.1)	37 (74.0)
	Median Survival Est. (95% CI)	0.59 (0.36, 0.95)	0.74 (0.33, 0.99)
	Hazard Ratio (95% CI)		0.835 (0.539, 1.294)
	Treatment P-value [a]		0.55306
	Interaction P-value [b]		0.60003
6 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.15 (0.06, 0.29)	3, 0.11 (0.04, 0.23)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.FS.KM.S10.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	132 (63.8)	120 (55.8)
	Median Survival Est. (95% CI)	0.76 (0.56, 0.95)	0.72 (0.49, 0.92)
	Hazard Ratio (95% CI)		0.956 (0.746, 1.224)
	Treatment P-value [a]		0.73652
	Interaction P-value [b]		0.60003
6 Months	Patients at Risk, Survival Est. (95% CI)	15, 0.20 (0.14, 0.28)	6, 0.14 (0.08, 0.22)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.12 (0.06, 0.20)	1, 0.14 (0.08, 0.22)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

2.4.1.2 Übelkeit und Erbrechen

Astellas: 7465-CL-0301
Table EORTC10.NVS.KM.S1.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	51 (47.2)	47 (42.3)
	Median Survival Est. (95% CI)	1.64 (0.95, 5.36)	2.14 (0.76, 4.86)
	Hazard Ratio (95% CI)		0.944 (0.634, 1.404)
	Treatment P-value [a]		0.80770
	Interaction P-value [b]		0.44357
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.38 (0.27, 0.49)	10, 0.37 (0.25, 0.50)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.NVS.KM.S1.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	89 (46.1)	94 (48.0)
	Median Survival Est. (95% CI)	1.87 (1.25, 2.63)	1.28 (0.85, 1.74)
	Hazard Ratio (95% CI)		0.779 (0.583, 1.041)
	Treatment P-value [a]		0.09270
	Interaction P-value [b]		0.44357
6 Months	Patients at Risk, Survival Est. (95% CI)	14, 0.36 (0.27, 0.44)	8, 0.27 (0.18, 0.37)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.27 (0.18, 0.37)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.NVS.KM.S2.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	122 (49.0)	112 (46.9)
	Median Survival Est. (95% CI)	1.68 (1.22, 2.37)	1.18 (0.82, 1.71)
	Hazard Ratio (95% CI)		0.797 (0.616, 1.030)
	Treatment P-value [a]		0.09288
	Interaction P-value [b]		0.74610
6 Months	Patients at Risk, Survival Est. (95% CI)	19, 0.36 (0.28, 0.43)	13, 0.29 (0.21, 0.37)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.NVS.KM.S2.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	18 (34.6)	29 (42.6)
	Median Survival Est. (95% CI)	2.37 (0.82, NC)	1.97 (0.99, NC)
	Hazard Ratio (95% CI)		0.886 (0.492, 1.596)
	Treatment P-value [a]		0.64696
	Interaction P-value [b]		0.74610
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.42 (0.23, 0.60)	5, 0.37 (0.21, 0.52)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.37 (0.21, 0.52)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.NVS.KM.S3.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	113 (47.5)	103 (44.4)
	Median Survival Est. (95% CI)	1.61 (1.18, 2.14)	1.48 (0.85, 1.97)
	Hazard Ratio (95% CI)		0.893 (0.683, 1.167)
	Treatment P-value [a]		0.42764
	Interaction P-value [b]		0.28523
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.35 (0.28, 0.43)	13, 0.34 (0.25, 0.43)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.NVS.KM.S3.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	27 (42.9)	38 (50.7)
	Median Survival Est. (95% CI)	2.60 (1.51, NC)	1.05 (0.82, 1.87)
	Hazard Ratio (95% CI)		0.657 (0.401, 1.078)
	Treatment P-value [a]		0.06724
	Interaction P-value [b]		0.28523
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.41 (0.26, 0.56)	5, 0.23 (0.11, 0.37)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.23 (0.11, 0.37)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.NVS.KM.S4.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	52 (41.3)	45 (34.9)
	Median Survival Est. (95% CI)	1.74 (0.95, NC)	1.41 (0.95, NC)
	Hazard Ratio (95% CI)		0.908 (0.609, 1.354)
	Treatment P-value [a]		0.59716
	Interaction P-value [b]		0.77826
6 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.40 (0.29, 0.51)	4, 0.41 (0.29, 0.52)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.41 (0.29, 0.52)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.NVS.KM.S4.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	16 (37.2)	17 (38.6)
	Median Survival Est. (95% CI)	1.22 (0.56, NC)	0.85 (0.62, NC)
	Hazard Ratio (95% CI)		0.932 (0.470, 1.850)
	Treatment P-value [a]		0.94181
	Interaction P-value [b]		0.77826
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.41 (0.22, 0.58)	3, 0.38 (0.20, 0.57)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.NVS.KM.S4.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	72 (54.5)	79 (59.0)
	Median Survival Est. (95% CI)	1.84 (1.18, 2.63)	1.25 (0.76, 1.97)
	Hazard Ratio (95% CI)		0.772 (0.561, 1.062)
	Treatment P-value [a]		0.11311
	Interaction P-value [b]		0.77826
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.33 (0.24, 0.43)	11, 0.25 (0.16, 0.35)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.NVS.KM.S5.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	57 (47.5)	64 (51.6)
	Median Survival Est. (95% CI)	2.37 (1.22, NC)	1.45 (0.82, 1.97)
	Hazard Ratio (95% CI)		0.743 (0.520, 1.062)
	Treatment P-value [a]		0.09191
	Interaction P-value [b]		0.40044
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.43 (0.33, 0.53)	10, 0.30 (0.20, 0.42)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.15 (0.02, 0.41)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.NVS.KM.S5.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	83 (45.9)	77 (42.1)
	Median Survival Est. (95% CI)	1.68 (1.05, 2.30)	1.18 (0.82, 2.14)
	Hazard Ratio (95% CI)		0.910 (0.667, 1.241)
	Treatment P-value [a]		0.60194
	Interaction P-value [b]		0.40044
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.31 (0.22, 0.40)	8, 0.31 (0.21, 0.41)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Astellas: 7465-CL-0301
Table EORTC10.NVS.KM.S6.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	44 (47.3)	42 (44.2)
	Median Survival Est. (95% CI)	1.45 (0.59, 2.37)	0.76 (0.36, 1.22)
	Hazard Ratio (95% CI)		0.778 (0.509, 1.188)
	Treatment P-value [a]		0.19912
	Interaction P-value [b]		0.74504
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.29 (0.17, 0.41)	4, 0.29 (0.18, 0.42)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.15 (0.02, 0.40)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.NVS.KM.S6.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	96 (46.2)	99 (46.7)
	Median Survival Est. (95% CI)	2.14 (1.41, 3.58)	1.74 (1.15, 3.55)
	Hazard Ratio (95% CI)		0.846 (0.639, 1.121)
	Treatment P-value [a]		0.27141
	Interaction P-value [b]		0.74504
6 Months	Patients at Risk, Survival Est. (95% CI)	15, 0.40 (0.31, 0.48)	14, 0.31 (0.23, 0.41)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.NVS.KM.S7.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	75 (53.2)	51 (45.5)
	Median Survival Est. (95% CI)	1.51 (0.85, 2.37)	1.45 (0.85, 3.78)
	Hazard Ratio (95% CI)		0.996 (0.698, 1.422)
	Treatment P-value [a]		0.99722
	Interaction P-value [b]		0.07770
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.31 (0.22, 0.41)	6, 0.29 (0.18, 0.42)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.NVS.KM.S7.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	34 (39.1)	61 (52.1)
	Median Survival Est. (95% CI)	3.98 (1.41, NC)	0.99 (0.62, 1.87)
	Hazard Ratio (95% CI)		0.555 (0.365, 0.845)
	Treatment P-value [a]		0.00669
	Interaction P-value [b]		0.07770
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.46 (0.33, 0.58)	8, 0.26 (0.15, 0.37)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.NVS.KM.S7.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	31 (42.5)	29 (37.2)
	Median Survival Est. (95% CI)	1.68 (0.99, NC)	1.74 (0.99, NC)
	Hazard Ratio (95% CI)		1.012 (0.609, 1.680)
	Treatment P-value [a]		0.96254
	Interaction P-value [b]		0.07770
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.37 (0.22, 0.51)	4, 0.44 (0.30, 0.57)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.44 (0.30, 0.57)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.NVS.KM.S8.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	47 (48.0)	58 (54.2)
	Median Survival Est. (95% CI)	1.45 (1.12, 1.84)	1.15 (0.62, 1.97)
	Hazard Ratio (95% CI)		0.852 (0.580, 1.253)
	Treatment P-value [a]		0.46632
	Interaction P-value [b]		0.93091
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.36 (0.25, 0.47)	9, 0.31 (0.21, 0.43)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.NVS.KM.S8.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	93 (45.8)	83 (41.5)
	Median Survival Est. (95% CI)	2.14 (1.25, 3.58)	1.48 (0.99, 2.14)
	Hazard Ratio (95% CI)		0.834 (0.620, 1.122)
	Treatment P-value [a]		0.22349
	Interaction P-value [b]		0.93091
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.37 (0.28, 0.45)	9, 0.30 (0.20, 0.41)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.26 (0.16, 0.38)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.NVS.KM.S9.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	121 (46.2)	126 (46.7)
	Median Survival Est. (95% CI)	1.84 (1.45, 2.60)	1.22 (0.99, 1.74)
	Hazard Ratio (95% CI)		0.791 (0.616, 1.016)
	Treatment P-value [a]		0.06548
	Interaction P-value [b]		0.26031
6 Months	Patients at Risk, Survival Est. (95% CI)	21, 0.37 (0.29, 0.44)	16, 0.30 (0.23, 0.38)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.09 (0.01, 0.29)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.NVS.KM.S9.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	19 (48.7)	15 (40.5)
	Median Survival Est. (95% CI)	1.41 (0.69, NC)	5.39 (0.39, NC)
	Hazard Ratio (95% CI)		1.198 (0.609, 2.358)
	Treatment P-value [a]		0.64190
	Interaction P-value [b]		0.26031
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.37 (0.20, 0.54)	2, 0.34 (0.09, 0.62)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.NVS.KM.S10.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	33 (54.1)	22 (44.0)
	Median Survival Est. (95% CI)	1.74 (1.22, 4.01)	1.91 (0.99, NC)
	Hazard Ratio (95% CI)		1.044 (0.609, 1.791)
	Treatment P-value [a]		0.82349
	Interaction P-value [b]		0.68524
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.34 (0.21, 0.48)	3, 0.41 (0.24, 0.57)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.NVS.KM.S10.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	100 (48.3)	98 (45.6)
	Median Survival Est. (95% CI)	1.25 (0.95, 1.87)	1.22 (0.82, 1.81)
	Hazard Ratio (95% CI)		0.921 (0.696, 1.218)
	Treatment P-value [a]		0.56450
	Interaction P-value [b]		0.68524
6 Months	Patients at Risk, Survival Est. (95% CI)	14, 0.33 (0.25, 0.41)	11, 0.27 (0.18, 0.37)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.14 (0.02, 0.38)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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2.4.1.3 Schmerz

Astellas: 7465-CL-0301
Table EORTC10.PS.KM.S1.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	60 (55.6)	53 (47.7)
	Median Survival Est. (95% CI)	0.99 (0.53, 2.14)	1.51 (0.99, 2.00)
	Hazard Ratio (95% CI)		1.048 (0.724, 1.518)
	Treatment P-value [a]		0.89863
	Interaction P-value [b]		0.17617
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.29 (0.17, 0.42)	5, 0.18 (0.08, 0.31)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.PS.KM.S1.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	105 (54.4)	106 (54.1)
	Median Survival Est. (95% CI)	1.25 (0.89, 1.64)	0.99 (0.56, 1.18)
	Hazard Ratio (95% CI)		0.764 (0.583, 1.002)
	Treatment P-value [a]		0.05970
	Interaction P-value [b]		0.17617
6 Months	Patients at Risk, Survival Est. (95% CI)	14, 0.29 (0.22, 0.37)	8, 0.19 (0.11, 0.27)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.25 (0.16, 0.34)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.PS.KM.S2.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	140 (56.2)	118 (49.4)
	Median Survival Est. (95% CI)	1.22 (0.89, 1.58)	1.18 (0.99, 1.61)
	Hazard Ratio (95% CI)		0.903 (0.706, 1.154)
	Treatment P-value [a]		0.40163
	Interaction P-value [b]		0.40849
6 Months	Patients at Risk, Survival Est. (95% CI)	18, 0.29 (0.22, 0.37)	10, 0.21 (0.13, 0.29)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.PS.KM.S2.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	25 (48.1)	41 (60.3)
	Median Survival Est. (95% CI)	1.05 (0.53, 3.68)	0.95 (0.43, 1.28)
	Hazard Ratio (95% CI)		0.714 (0.434, 1.175)
	Treatment P-value [a]		0.18852
	Interaction P-value [b]		0.40849
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.31 (0.16, 0.47)	3, 0.13 (0.05, 0.26)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.31 (0.16, 0.47)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Astellas: 7465-CL-0301
Table EORTC10.PS.KM.S3.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	135 (56.7)	120 (51.7)
	Median Survival Est. (95% CI)	1.02 (0.82, 1.48)	1.18 (0.95, 1.51)
	Hazard Ratio (95% CI)		0.907 (0.709, 1.160)
	Treatment P-value [a]		0.44362
	Interaction P-value [b]		0.29656
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.27 (0.20, 0.35)	10, 0.19 (0.12, 0.27)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.18 (0.11, 0.27)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.PS.KM.S3.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	30 (47.6)	39 (52.0)
	Median Survival Est. (95% CI)	1.48 (0.85, 9.99)	0.99 (0.79, 1.54)
	Hazard Ratio (95% CI)		0.681 (0.423, 1.098)
	Treatment P-value [a]		0.09507
	Interaction P-value [b]		0.29656
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.37 (0.22, 0.53)	3, 0.18 (0.08, 0.33)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Astellas: 7465-CL-0301
Table EORTC10.PS.KM.S4.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	60 (47.6)	58 (45.0)
	Median Survival Est. (95% CI)	1.05 (0.76, 2.14)	0.99 (0.43, 1.22)
	Hazard Ratio (95% CI)		0.738 (0.514, 1.060)
	Treatment P-value [a]		0.12427
	Interaction P-value [b]		0.54128
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.35 (0.23, 0.47)	5, 0.21 (0.12, 0.31)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.PS.KM.S4.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	20 (46.5)	18 (40.9)
	Median Survival Est. (95% CI)	1.58 (0.62, 3.68)	1.02 (0.76, 2.69)
	Hazard Ratio (95% CI)		0.831 (0.438, 1.575)
	Treatment P-value [a]		0.62359
	Interaction P-value [b]		0.54128
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.27 (0.11, 0.45)	1, 0.27 (0.11, 0.45)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.27 (0.11, 0.45)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.PS.KM.S4.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	85 (64.4)	83 (61.9)
	Median Survival Est. (95% CI)	1.02 (0.79, 1.48)	1.25 (0.95, 1.68)
	Hazard Ratio (95% CI)		0.963 (0.711, 1.303)
	Treatment P-value [a]		0.87477
	Interaction P-value [b]		0.54128
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.27 (0.19, 0.36)	7, 0.17 (0.09, 0.27)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.PS.KM.S5.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	70 (58.3)	72 (58.1)
	Median Survival Est. (95% CI)	1.45 (0.89, 2.14)	1.22 (0.85, 1.68)
	Hazard Ratio (95% CI)		0.843 (0.606, 1.172)
	Treatment P-value [a]		0.25136
	Interaction P-value [b]		0.91829
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.32 (0.21, 0.43)	5, 0.18 (0.09, 0.29)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.PS.KM.S5.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	95 (52.5)	87 (47.5)
	Median Survival Est. (95% CI)	1.02 (0.76, 1.48)	0.99 (0.72, 1.25)
	Hazard Ratio (95% CI)		0.863 (0.645, 1.154)
	Treatment P-value [a]		0.34841
	Interaction P-value [b]		0.91829
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.28 (0.20, 0.37)	8, 0.19 (0.11, 0.29)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.25 (0.17, 0.35)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.PS.KM.S6.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	48 (51.6)	43 (45.3)
	Median Survival Est. (95% CI)	1.38 (0.82, 2.14)	0.99 (0.69, 1.38)
	Hazard Ratio (95% CI)		0.780 (0.516, 1.180)
	Treatment P-value [a]		0.26789
	Interaction P-value [b]		0.60611
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.30 (0.18, 0.42)	2, 0.18 (0.08, 0.32)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.17 (0.05, 0.36)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.PS.KM.S6.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	117 (56.3)	116 (54.7)
	Median Survival Est. (95% CI)	1.05 (0.82, 1.61)	1.18 (0.95, 1.61)
	Hazard Ratio (95% CI)		0.886 (0.686, 1.146)
	Treatment P-value [a]		0.38652
	Interaction P-value [b]		0.60611
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.29 (0.21, 0.37)	11, 0.19 (0.12, 0.27)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.PS.KM.S7.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	82 (58.2)	56 (50.0)
	Median Survival Est. (95% CI)	0.99 (0.79, 1.48)	1.18 (0.69, 1.68)
	Hazard Ratio (95% CI)		0.944 (0.672, 1.326)
	Treatment P-value [a]		0.75856
	Interaction P-value [b]		0.45954
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.30 (0.22, 0.39)	4, 0.20 (0.11, 0.32)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.PS.KM.S7.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	51 (58.6)	65 (55.6)
	Median Survival Est. (95% CI)	1.41 (0.59, 1.64)	1.02 (0.85, 1.51)
	Hazard Ratio (95% CI)		0.903 (0.625, 1.304)
	Treatment P-value [a]		0.52777
	Interaction P-value [b]		0.45954
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.22 (0.13, 0.34)	5, 0.15 (0.07, 0.27)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.18 (0.08, 0.31)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Astellas: 7465-CL-0301
Table EORTC10.PS.KM.S7.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	32 (43.8)	38 (48.7)
	Median Survival Est. (95% CI)	2.14 (0.85, 6.21)	1.15 (0.53, 1.51)
	Hazard Ratio (95% CI)		0.661 (0.413, 1.058)
	Treatment P-value [a]		0.10094
	Interaction P-value [b]		0.45954
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.37 (0.20, 0.54)	4, 0.23 (0.11, 0.36)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.PS.KM.S8.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	49 (50.0)	66 (61.7)
	Median Survival Est. (95% CI)	1.41 (0.82, 5.36)	0.99 (0.53, 1.25)
	Hazard Ratio (95% CI)		0.702 (0.484, 1.016)
	Treatment P-value [a]		0.06014
	Interaction P-value [b]		0.18482
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.36 (0.25, 0.48)	4, 0.16 (0.07, 0.27)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.PS.KM.S8.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	116 (57.1)	93 (46.5)
	Median Survival Est. (95% CI)	1.05 (0.82, 1.51)	1.22 (0.99, 1.54)
	Hazard Ratio (95% CI)		0.958 (0.729, 1.259)
	Treatment P-value [a]		0.82331
	Interaction P-value [b]		0.18482
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.26 (0.18, 0.35)	9, 0.21 (0.13, 0.30)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.21 (0.13, 0.31)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.PS.KM.S9.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	145 (55.3)	139 (51.5)
	Median Survival Est. (95% CI)	1.08 (0.89, 1.51)	1.08 (0.95, 1.28)
	Hazard Ratio (95% CI)		0.839 (0.665, 1.060)
	Treatment P-value [a]		0.14154
	Interaction P-value [b]		0.69561
6 Months	Patients at Risk, Survival Est. (95% CI)	18, 0.28 (0.21, 0.35)	11, 0.19 (0.13, 0.26)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.17 (0.08, 0.28)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.PS.KM.S9.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	20 (51.3)	20 (54.1)
	Median Survival Est. (95% CI)	1.45 (0.36, NC)	1.45 (0.72, 5.39)
	Hazard Ratio (95% CI)		0.958 (0.515, 1.782)
	Treatment P-value [a]		0.81413
	Interaction P-value [b]		0.69561
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.41 (0.24, 0.57)	2, 0.17 (0.04, 0.39)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.PS.KM.S10.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	39 (63.9)	34 (68.0)
	Median Survival Est. (95% CI)	1.22 (0.82, 1.71)	0.99 (0.36, 1.45)
	Hazard Ratio (95% CI)		0.743 (0.469, 1.177)
	Treatment P-value [a]		0.19900
	Interaction P-value [b]		0.25561
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.16 (0.04, 0.33)	2, 0.09 (0.02, 0.23)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.PS.KM.S10.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	112 (54.1)	101 (47.0)
	Median Survival Est. (95% CI)	0.99 (0.76, 1.48)	1.22 (1.02, 1.71)
	Hazard Ratio (95% CI)		1.013 (0.773, 1.326)
	Treatment P-value [a]		0.91083
	Interaction P-value [b]		0.25561
6 Months	Patients at Risk, Survival Est. (95% CI)	18, 0.31 (0.23, 0.39)	10, 0.24 (0.16, 0.33)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.17 (0.07, 0.31)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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2.4.1.4 Atemnot

Astellas: 7465-CL-0301
Table EORTC10.DS.KM.S1.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	42 (38.9)	39 (35.1)
	Median Survival Est. (95% CI)	5.45 (1.45, NC)	3.78 (1.71, 8.05)
	Hazard Ratio (95% CI)		0.936 (0.605, 1.448)
	Treatment P-value [a]		0.76028
	Interaction P-value [b]		0.27212
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.49 (0.36, 0.60)	10, 0.43 (0.30, 0.56)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.42 (0.26, 0.57)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.DS.KM.S1.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	76 (39.4)	91 (46.4)
	Median Survival Est. (95% CI)	3.58 (1.64, NC)	1.51 (1.18, 2.33)
	Hazard Ratio (95% CI)		0.695 (0.512, 0.943)
	Treatment P-value [a]		0.01726
	Interaction P-value [b]		0.27212
6 Months	Patients at Risk, Survival Est. (95% CI)	18, 0.46 (0.37, 0.55)	7, 0.27 (0.18, 0.37)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.40 (0.26, 0.53)	3, 0.27 (0.18, 0.37)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.DS.KM.S2.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	98 (39.4)	96 (40.2)
	Median Survival Est. (95% CI)	5.45 (1.71, NC)	2.33 (1.68, 3.78)
	Hazard Ratio (95% CI)		0.780 (0.588, 1.033)
	Treatment P-value [a]		0.08601
	Interaction P-value [b]		0.95375
6 Months	Patients at Risk, Survival Est. (95% CI)	27, 0.49 (0.41, 0.56)	13, 0.33 (0.24, 0.42)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.46 (0.37, 0.55)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.DS.KM.S2.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	20 (38.5)	34 (50.0)
	Median Survival Est. (95% CI)	2.60 (1.02, NC)	1.28 (0.99, 2.23)
	Hazard Ratio (95% CI)		0.765 (0.440, 1.330)
	Treatment P-value [a]		0.33048
	Interaction P-value [b]		0.95375
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.38 (0.19, 0.57)	4, 0.29 (0.16, 0.44)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.25 (0.06, 0.50)	3, 0.29 (0.16, 0.44)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.DS.KM.S3.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	95 (39.9)	103 (44.4)
	Median Survival Est. (95% CI)	4.44 (1.64, NC)	1.68 (1.22, 2.43)
	Hazard Ratio (95% CI)		0.726 (0.549, 0.959)
	Treatment P-value [a]		0.02205
	Interaction P-value [b]		0.48967
6 Months	Patients at Risk, Survival Est. (95% CI)	24, 0.47 (0.39, 0.55)	12, 0.30 (0.21, 0.39)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.39 (0.26, 0.51)	2, 0.23 (0.14, 0.34)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.DS.KM.S3.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	23 (36.5)	27 (36.0)
	Median Survival Est. (95% CI)	3.58 (1.61, NC)	2.46 (1.68, NC)
	Hazard Ratio (95% CI)		0.903 (0.518, 1.576)
	Treatment P-value [a]		0.74169
	Interaction P-value [b]		0.48967
6 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.49 (0.33, 0.63)	5, 0.42 (0.26, 0.56)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.42 (0.26, 0.56)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.DS.KM.S4.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	40 (31.7)	50 (38.8)
	Median Survival Est. (95% CI)	NC (1.68, NC)	1.28 (0.79, 2.66)
	Hazard Ratio (95% CI)		0.568 (0.374, 0.861)
	Treatment P-value [a]		0.00997
	Interaction P-value [b]		0.20390
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.52 (0.39, 0.64)	6, 0.29 (0.17, 0.41)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	2, 0.29 (0.17, 0.41)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.DS.KM.S4.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	13 (30.2)	14 (31.8)
	Median Survival Est. (95% CI)	NC (0.82, NC)	2.60 (1.12, NC)
	Hazard Ratio (95% CI)		0.849 (0.398, 1.813)
	Treatment P-value [a]		0.86901
	Interaction P-value [b]		0.20390
6 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.51 (0.30, 0.68)	2, 0.37 (0.16, 0.58)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.51 (0.30, 0.68)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.DS.KM.S4.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	65 (49.2)	66 (49.3)
	Median Survival Est. (95% CI)	2.60 (1.61, 7.56)	2.33 (1.51, 4.37)
	Hazard Ratio (95% CI)		0.922 (0.654, 1.299)
	Treatment P-value [a]		0.63409
	Interaction P-value [b]		0.20390
6 Months	Patients at Risk, Survival Est. (95% CI)	16, 0.43 (0.33, 0.52)	9, 0.34 (0.24, 0.45)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.25 (0.08, 0.48)	1, 0.25 (0.13, 0.39)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.DS.KM.S5.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	42 (35.0)	58 (46.8)
	Median Survival Est. (95% CI)	NC (5.36, NC)	2.37 (1.61, 4.60)
	Hazard Ratio (95% CI)		0.625 (0.420, 0.930)
	Treatment P-value [a]		0.01437
	Interaction P-value [b]		0.19721
6 Months	Patients at Risk, Survival Est. (95% CI)	19, 0.57 (0.45, 0.67)	7, 0.35 (0.24, 0.47)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.53 (0.40, 0.64)	1, 0.25 (0.13, 0.40)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.DS.KM.S5.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	76 (42.0)	72 (39.3)
	Median Survival Est. (95% CI)	1.71 (1.28, 4.44)	1.71 (1.02, 2.66)
	Hazard Ratio (95% CI)		0.875 (0.634, 1.208)
	Treatment P-value [a]		0.40971
	Interaction P-value [b]		0.19721
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.40 (0.31, 0.49)	10, 0.30 (0.20, 0.41)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.32 (0.17, 0.48)	2, 0.30 (0.20, 0.41)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.DS.KM.S6.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	35 (37.6)	38 (40.0)
	Median Survival Est. (95% CI)	2.60 (1.38, NC)	1.51 (1.12, 2.66)
	Hazard Ratio (95% CI)		0.717 (0.453, 1.136)
	Treatment P-value [a]		0.16642
	Interaction P-value [b]		0.74224
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.45 (0.31, 0.58)	3, 0.25 (0.12, 0.40)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.45 (0.31, 0.58)	2, 0.25 (0.12, 0.40)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.DS.KM.S6.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	83 (39.9)	92 (43.4)
	Median Survival Est. (95% CI)	4.44 (1.71, NC)	2.23 (1.68, 4.17)
	Hazard Ratio (95% CI)		0.786 (0.584, 1.058)
	Treatment P-value [a]		0.11947
	Interaction P-value [b]		0.74224
6 Months	Patients at Risk, Survival Est. (95% CI)	21, 0.49 (0.40, 0.57)	14, 0.35 (0.26, 0.44)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.39 (0.25, 0.53)	1, 0.29 (0.19, 0.40)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.DS.KM.S7.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	63 (44.7)	45 (40.2)
	Median Survival Est. (95% CI)	2.66 (1.54, 7.56)	2.10 (1.48, 4.37)
	Hazard Ratio (95% CI)		0.922 (0.629, 1.352)
	Treatment P-value [a]		0.66552
	Interaction P-value [b]		0.20802
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.42 (0.31, 0.52)	7, 0.34 (0.21, 0.46)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.28 (0.12, 0.47)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.DS.KM.S7.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	35 (40.2)	51 (43.6)
	Median Survival Est. (95% CI)	2.46 (1.41, NC)	1.94 (1.25, 5.36)
	Hazard Ratio (95% CI)		0.787 (0.512, 1.211)
	Treatment P-value [a]		0.27620
	Interaction P-value [b]		0.20802
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.47 (0.35, 0.59)	6, 0.32 (0.19, 0.45)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.47 (0.35, 0.59)	1, 0.27 (0.13, 0.42)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.DS.KM.S7.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	20 (27.4)	34 (43.6)
	Median Survival Est. (95% CI)	NC (1.68, NC)	1.71 (0.79, 3.19)
	Hazard Ratio (95% CI)		0.503 (0.290, 0.874)
	Treatment P-value [a]		0.01430
	Interaction P-value [b]		0.20802
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.62 (0.47, 0.74)	4, 0.31 (0.18, 0.45)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	2, 0.31 (0.18, 0.45)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.DS.KM.S8.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	45 (45.9)	53 (49.5)
	Median Survival Est. (95% CI)	1.64 (1.02, 5.36)	1.68 (1.25, 2.46)
	Hazard Ratio (95% CI)		0.958 (0.644, 1.425)
	Treatment P-value [a]		0.86422
	Interaction P-value [b]		0.21595
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.37 (0.25, 0.48)	6, 0.28 (0.17, 0.41)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.27 (0.12, 0.46)	1, 0.24 (0.12, 0.38)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.DS.KM.S8.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	73 (36.0)	77 (38.5)
	Median Survival Est. (95% CI)	9.36 (2.63, NC)	2.23 (1.38, 4.17)
	Hazard Ratio (95% CI)		0.694 (0.504, 0.956)
	Treatment P-value [a]		0.02865
	Interaction P-value [b]		0.21595
6 Months	Patients at Risk, Survival Est. (95% CI)	21, 0.52 (0.43, 0.60)	11, 0.35 (0.26, 0.45)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.46 (0.31, 0.59)	2, 0.31 (0.20, 0.43)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.DS.KM.S9.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	100 (38.2)	110 (40.7)
	Median Survival Est. (95% CI)	5.36 (1.91, NC)	2.17 (1.48, 2.83)
	Hazard Ratio (95% CI)		0.761 (0.580, 0.998)
	Treatment P-value [a]		0.05157
	Interaction P-value [b]		0.84749
6 Months	Patients at Risk, Survival Est. (95% CI)	29, 0.49 (0.42, 0.56)	16, 0.34 (0.25, 0.42)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.42 (0.30, 0.53)	2, 0.28 (0.19, 0.38)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.DS.KM.S9.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	18 (46.2)	20 (54.1)
	Median Survival Est. (95% CI)	1.71 (0.82, NC)	1.94 (1.02, 4.60)
	Hazard Ratio (95% CI)		0.815 (0.430, 1.545)
	Treatment P-value [a]		0.52896
	Interaction P-value [b]		0.84749
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.36 (0.17, 0.56)	1, 0.25 (0.09, 0.45)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.25 (0.09, 0.45)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.DS.KM.S10.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	24 (39.3)	26 (52.0)
	Median Survival Est. (95% CI)	NC (1.64, NC)	1.68 (0.99, 7.46)
	Hazard Ratio (95% CI)		0.590 (0.339, 1.028)
	Treatment P-value [a]		0.06780
	Interaction P-value [b]		0.13424
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.52 (0.37, 0.65)	4, 0.35 (0.20, 0.51)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.DS.KM.S10.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	87 (42.0)	84 (39.1)
	Median Survival Est. (95% CI)	2.50 (1.45, 7.56)	2.43 (1.68, 4.37)
	Hazard Ratio (95% CI)		0.956 (0.708, 1.290)
	Treatment P-value [a]		0.72682
	Interaction P-value [b]		0.13424
6 Months	Patients at Risk, Survival Est. (95% CI)	20, 0.42 (0.33, 0.51)	11, 0.33 (0.23, 0.43)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.33 (0.20, 0.47)	3, 0.33 (0.23, 0.43)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

2.4.1.5 Schlaflosigkeit

Astellas: 7465-CL-0301
Table EORTC10.SLS.KM.S1.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	51 (47.2)	41 (36.9)
	Median Survival Est. (95% CI)	1.91 (0.76, 6.54)	2.46 (1.71, 7.46)
	Hazard Ratio (95% CI)		1.222 (0.810, 1.844)
	Treatment P-value [a]		0.35139
	Interaction P-value [b]		0.05953
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.38 (0.26, 0.51)	8, 0.38 (0.24, 0.52)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.SLS.KM.S1.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	88 (45.6)	93 (47.4)
	Median Survival Est. (95% CI)	1.68 (1.05, 5.52)	1.15 (0.82, 1.74)
	Hazard Ratio (95% CI)		0.752 (0.562, 1.008)
	Treatment P-value [a]		0.05980
	Interaction P-value [b]		0.05953
6 Months	Patients at Risk, Survival Est. (95% CI)	16, 0.35 (0.25, 0.45)	9, 0.29 (0.20, 0.39)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.30 (0.19, 0.41)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.SLS.KM.S2.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	120 (48.2)	96 (40.2)
	Median Survival Est. (95% CI)	1.81 (1.05, 2.60)	1.94 (1.18, 4.17)
	Hazard Ratio (95% CI)		1.017 (0.777, 1.330)
	Treatment P-value [a]		0.89903
	Interaction P-value [b]		0.05367
6 Months	Patients at Risk, Survival Est. (95% CI)	20, 0.36 (0.27, 0.44)	14, 0.36 (0.27, 0.46)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.25 (0.15, 0.37)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.SLS.KM.S2.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	19 (36.5)	38 (55.9)
	Median Survival Est. (95% CI)	2.23 (0.99, NC)	0.99 (0.56, 1.68)
	Hazard Ratio (95% CI)		0.556 (0.320, 0.965)
	Treatment P-value [a]		0.03722
	Interaction P-value [b]		0.05367
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.37 (0.15, 0.60)	3, 0.20 (0.09, 0.35)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.37 (0.15, 0.60)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Astellas: 7465-CL-0301
Table EORTC10.SLS.KM.S3.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	114 (47.9)	101 (43.5)
	Median Survival Est. (95% CI)	1.45 (0.99, 2.23)	1.45 (1.02, 2.37)
	Hazard Ratio (95% CI)		0.952 (0.728, 1.244)
	Treatment P-value [a]		0.73032
	Interaction P-value [b]		0.30174
6 Months	Patients at Risk, Survival Est. (95% CI)	19, 0.35 (0.27, 0.43)	14, 0.33 (0.24, 0.42)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.28 (0.19, 0.38)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.SLS.KM.S3.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	25 (39.7)	33 (44.0)
	Median Survival Est. (95% CI)	5.52 (1.15, NC)	1.77 (1.08, 2.46)
	Hazard Ratio (95% CI)		0.699 (0.416, 1.176)
	Treatment P-value [a]		0.15411
	Interaction P-value [b]		0.30174
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.38 (0.17, 0.59)	3, 0.29 (0.15, 0.45)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.SLS.KM.S4.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	49 (38.9)	54 (41.9)
	Median Survival Est. (95% CI)	2.40 (1.28, 9.07)	0.99 (0.39, 1.48)
	Hazard Ratio (95% CI)		0.577 (0.392, 0.850)
	Treatment P-value [a]		0.00594
	Interaction P-value [b]		0.01354
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.41 (0.27, 0.55)	4, 0.27 (0.17, 0.38)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.SLS.KM.S4.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	15 (34.9)	17 (38.6)
	Median Survival Est. (95% CI)	1.87 (1.05, NC)	1.74 (0.82, 7.69)
	Hazard Ratio (95% CI)		0.807 (0.403, 1.618)
	Treatment P-value [a]		0.60672
	Interaction P-value [b]		0.01354
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.43 (0.23, 0.61)	2, 0.37 (0.18, 0.55)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.43 (0.23, 0.61)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.SLS.KM.S4.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	75 (56.8)	63 (47.0)
	Median Survival Est. (95% CI)	1.05 (0.89, 2.60)	2.46 (1.25, 5.39)
	Hazard Ratio (95% CI)		1.239 (0.886, 1.733)
	Treatment P-value [a]		0.26483
	Interaction P-value [b]		0.01354
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.31 (0.21, 0.42)	11, 0.35 (0.23, 0.47)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.25 (0.15, 0.37)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.SLS.KM.S5.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	63 (52.5)	57 (46.0)
	Median Survival Est. (95% CI)	1.45 (0.99, 5.68)	2.33 (1.05, 5.45)
	Hazard Ratio (95% CI)		0.991 (0.692, 1.419)
	Treatment P-value [a]		0.84496
	Interaction P-value [b]		0.44503
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.37 (0.26, 0.49)	6, 0.34 (0.20, 0.48)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.24 (0.11, 0.40)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.SLS.KM.S5.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	76 (42.0)	77 (42.1)
	Median Survival Est. (95% CI)	1.91 (1.02, 5.52)	1.31 (0.99, 1.87)
	Hazard Ratio (95% CI)		0.822 (0.599, 1.129)
	Treatment P-value [a]		0.21142
	Interaction P-value [b]		0.44503
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.35 (0.24, 0.46)	11, 0.29 (0.20, 0.39)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.31 (0.19, 0.43)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.SLS.KM.S6.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	40 (43.0)	43 (45.3)
	Median Survival Est. (95% CI)	1.31 (0.99, 6.54)	0.99 (0.53, 1.22)
	Hazard Ratio (95% CI)		0.619 (0.402, 0.954)
	Treatment P-value [a]		0.02593
	Interaction P-value [b]		0.05921
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.37 (0.24, 0.51)	1, 0.13 (0.02, 0.37)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.22 (0.06, 0.43)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.SLS.KM.S6.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	99 (47.6)	91 (42.9)
	Median Survival Est. (95% CI)	1.87 (1.05, 5.42)	1.94 (1.25, 4.37)
	Hazard Ratio (95% CI)		1.019 (0.766, 1.354)
	Treatment P-value [a]		0.89753
	Interaction P-value [b]		0.05921
6 Months	Patients at Risk, Survival Est. (95% CI)	15, 0.35 (0.25, 0.45)	16, 0.37 (0.28, 0.46)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.29 (0.19, 0.40)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.SLS.KM.S7.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	70 (49.6)	42 (37.5)
	Median Survival Est. (95% CI)	1.08 (0.89, 2.60)	2.43 (1.02, 7.69)
	Hazard Ratio (95% CI)		1.136 (0.774, 1.667)
	Treatment P-value [a]		0.49503
	Interaction P-value [b]		0.14729
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.35 (0.24, 0.45)	5, 0.35 (0.19, 0.51)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.31 (0.20, 0.43)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.SLS.KM.S7.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	41 (47.1)	57 (48.7)
	Median Survival Est. (95% CI)	1.81 (0.99, 5.52)	1.71 (1.05, 2.46)
	Hazard Ratio (95% CI)		0.895 (0.599, 1.337)
	Treatment P-value [a]		0.55689
	Interaction P-value [b]		0.14729
6 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.34 (0.20, 0.49)	8, 0.29 (0.18, 0.41)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.29 (0.14, 0.45)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.SLS.KM.S7.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	28 (38.4)	35 (44.9)
	Median Survival Est. (95% CI)	5.42 (1.28, 9.07)	1.02 (0.53, 1.77)
	Hazard Ratio (95% CI)		0.607 (0.369, 0.998)
	Treatment P-value [a]		0.04774
	Interaction P-value [b]		0.14729
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.39 (0.20, 0.58)	4, 0.31 (0.19, 0.45)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.SLS.KM.S8.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	46 (46.9)	58 (54.2)
	Median Survival Est. (95% CI)	1.41 (0.85, 6.54)	1.08 (0.82, 1.74)
	Hazard Ratio (95% CI)		0.787 (0.534, 1.161)
	Treatment P-value [a]		0.21710
	Interaction P-value [b]		0.38359
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.38 (0.25, 0.50)	5, 0.25 (0.13, 0.39)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.23 (0.07, 0.44)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.SLS.KM.S8.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	93 (45.8)	76 (38.0)
	Median Survival Est. (95% CI)	1.91 (1.05, 5.42)	1.87 (1.18, 4.37)
	Hazard Ratio (95% CI)		0.980 (0.724, 1.328)
	Treatment P-value [a]		0.93695
	Interaction P-value [b]		0.38359
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.34 (0.24, 0.45)	12, 0.36 (0.26, 0.46)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.27 (0.16, 0.40)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.SLS.KM.S9.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	120 (45.8)	117 (43.3)
	Median Survival Est. (95% CI)	1.81 (1.05, 5.42)	1.31 (1.02, 2.37)
	Hazard Ratio (95% CI)		0.878 (0.681, 1.134)
	Treatment P-value [a]		0.31791
	Interaction P-value [b]		0.72072
6 Months	Patients at Risk, Survival Est. (95% CI)	21, 0.37 (0.28, 0.45)	15, 0.33 (0.25, 0.41)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.29 (0.18, 0.39)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.SLS.KM.S9.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	19 (48.7)	17 (45.9)
	Median Survival Est. (95% CI)	1.81 (0.99, 6.54)	1.94 (0.82, NC)
	Hazard Ratio (95% CI)		0.998 (0.519, 1.921)
	Treatment P-value [a]		0.89969
	Interaction P-value [b]		0.72072
6 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.32 (0.12, 0.55)	2, 0.27 (0.07, 0.53)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.SLS.KM.S10.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	38 (62.3)	24 (48.0)
	Median Survival Est. (95% CI)	1.02 (0.59, 1.68)	1.84 (0.99, 7.46)
	Hazard Ratio (95% CI)		1.402 (0.840, 2.340)
	Treatment P-value [a]		0.15625
	Interaction P-value [b]		0.05847
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.15 (0.02, 0.41)	5, 0.38 (0.23, 0.54)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.SLS.KM.S10.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	90 (43.5)	95 (44.2)
	Median Survival Est. (95% CI)	1.91 (1.05, 5.42)	1.22 (0.99, 2.37)
	Hazard Ratio (95% CI)		0.794 (0.595, 1.060)
	Treatment P-value [a]		0.12018
	Interaction P-value [b]		0.05847
6 Months	Patients at Risk, Survival Est. (95% CI)	19, 0.39 (0.30, 0.48)	10, 0.28 (0.19, 0.38)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.31 (0.19, 0.44)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

2.4.1.6 Appetitverlust

Astellas: 7465-CL-0301
Table EORTC10.APS.KM.S1.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	55 (50.9)	47 (42.3)
	Median Survival Est. (95% CI)	1.51 (0.79, 5.32)	1.05 (0.62, 5.32)
	Hazard Ratio (95% CI)		0.938 (0.636, 1.385)
	Treatment P-value [a]		0.69871
	Interaction P-value [b]		0.77857
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.38 (0.27, 0.49)	5, 0.30 (0.16, 0.45)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.APS.KM.S1.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	109 (56.5)	95 (48.5)
	Median Survival Est. (95% CI)	0.99 (0.76, 1.28)	1.18 (0.76, 1.71)
	Hazard Ratio (95% CI)		1.005 (0.763, 1.324)
	Treatment P-value [a]		0.90433
	Interaction P-value [b]		0.77857
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.27 (0.19, 0.35)	8, 0.26 (0.17, 0.35)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	2, 0.26 (0.17, 0.35)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.APS.KM.S2.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	137 (55.0)	104 (43.5)
	Median Survival Est. (95% CI)	1.25 (0.95, 1.64)	1.15 (0.79, 1.87)
	Hazard Ratio (95% CI)		0.967 (0.749, 1.249)
	Treatment P-value [a]		0.82394
	Interaction P-value [b]		0.55486
6 Months	Patients at Risk, Survival Est. (95% CI)	16, 0.31 (0.24, 0.39)	8, 0.30 (0.20, 0.40)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.APS.KM.S2.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	27 (51.9)	38 (55.9)
	Median Survival Est. (95% CI)	0.56 (0.49, 1.08)	1.08 (0.56, 1.77)
	Hazard Ratio (95% CI)		1.144 (0.698, 1.876)
	Treatment P-value [a]		0.65871
	Interaction P-value [b]		0.55486
6 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.30 (0.16, 0.44)	5, 0.22 (0.11, 0.35)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	2, 0.22 (0.11, 0.35)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.APS.KM.S3.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	136 (57.1)	102 (44.0)
	Median Survival Est. (95% CI)	0.99 (0.76, 1.28)	1.51 (0.99, 1.97)
	Hazard Ratio (95% CI)		1.129 (0.873, 1.460)
	Treatment P-value [a]		0.34647
	Interaction P-value [b]		0.02192
6 Months	Patients at Risk, Survival Est. (95% CI)	14, 0.28 (0.21, 0.35)	9, 0.30 (0.20, 0.39)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.26 (0.16, 0.37)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.APS.KM.S3.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	28 (44.4)	40 (53.3)
	Median Survival Est. (95% CI)	1.68 (0.82, NC)	0.99 (0.62, 1.15)
	Hazard Ratio (95% CI)		0.595 (0.367, 0.965)
	Treatment P-value [a]		0.02432
	Interaction P-value [b]		0.02192
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.43 (0.27, 0.57)	4, 0.19 (0.09, 0.33)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.19 (0.09, 0.33)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.APS.KM.S4.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	58 (46.0)	47 (36.4)
	Median Survival Est. (95% CI)	1.51 (0.89, 5.32)	1.51 (0.66, 2.37)
	Hazard Ratio (95% CI)		0.962 (0.655, 1.414)
	Treatment P-value [a]		0.83977
	Interaction P-value [b]		0.31220
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.33 (0.21, 0.46)	5, 0.35 (0.23, 0.47)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.35 (0.23, 0.47)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.APS.KM.S4.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	21 (48.8)	14 (31.8)
	Median Survival Est. (95% CI)	1.05 (0.53, NC)	2.56 (1.02, NC)
	Hazard Ratio (95% CI)		1.584 (0.805, 3.117)
	Treatment P-value [a]		0.10671
	Interaction P-value [b]		0.31220
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.36 (0.20, 0.53)	2, 0.42 (0.22, 0.61)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.APS.KM.S4.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	85 (64.4)	81 (60.4)
	Median Survival Est. (95% CI)	0.99 (0.62, 1.41)	0.99 (0.43, 1.38)
	Hazard Ratio (95% CI)		0.890 (0.656, 1.207)
	Treatment P-value [a]		0.44123
	Interaction P-value [b]		0.31220
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.26 (0.18, 0.35)	6, 0.20 (0.11, 0.31)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.15 (0.06, 0.28)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.APS.KM.S5.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	74 (61.7)	65 (52.4)
	Median Survival Est. (95% CI)	1.08 (0.76, 1.54)	1.02 (0.62, 1.87)
	Hazard Ratio (95% CI)		0.970 (0.695, 1.354)
	Treatment P-value [a]		0.82584
	Interaction P-value [b]		0.94206
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.29 (0.20, 0.38)	5, 0.28 (0.16, 0.42)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.21 (0.08, 0.38)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.APS.KM.S5.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	90 (49.7)	77 (42.1)
	Median Survival Est. (95% CI)	1.25 (0.79, 1.71)	1.28 (0.76, 1.94)
	Hazard Ratio (95% CI)		0.986 (0.727, 1.337)
	Treatment P-value [a]		0.93101
	Interaction P-value [b]		0.94206
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.33 (0.24, 0.42)	8, 0.26 (0.17, 0.36)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.26 (0.17, 0.36)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Astellas: 7465-CL-0301
Table EORTC10.APS.KM.S6.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	43 (46.2)	39 (41.1)
	Median Survival Est. (95% CI)	1.28 (0.69, 9.07)	1.28 (0.66, 2.10)
	Hazard Ratio (95% CI)		0.851 (0.551, 1.313)
	Treatment P-value [a]		0.45140
	Interaction P-value [b]		0.45229
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.40 (0.28, 0.51)	2, 0.23 (0.10, 0.38)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.23 (0.10, 0.38)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.APS.KM.S6.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	121 (58.2)	103 (48.6)
	Median Survival Est. (95% CI)	1.02 (0.79, 1.51)	1.05 (0.76, 1.87)
	Hazard Ratio (95% CI)		1.034 (0.795, 1.345)
	Treatment P-value [a]		0.76685
	Interaction P-value [b]		0.45229
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.27 (0.20, 0.35)	11, 0.29 (0.21, 0.38)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.26 (0.17, 0.36)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.APS.KM.S7.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	83 (58.9)	43 (38.4)
	Median Survival Est. (95% CI)	1.02 (0.76, 1.54)	1.91 (1.18, NC)
	Hazard Ratio (95% CI)		1.381 (0.955, 1.996)
	Treatment P-value [a]		0.07220
	Interaction P-value [b]		0.06687
6 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.26 (0.16, 0.36)	5, 0.38 (0.26, 0.51)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Table EORTC10.APS.KM.S7.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	47 (54.0)	63 (53.8)
	Median Survival Est. (95% CI)	1.02 (0.56, 1.64)	0.99 (0.36, 1.08)
	Hazard Ratio (95% CI)		0.760 (0.521, 1.110)
	Treatment P-value [a]		0.15958
	Interaction P-value [b]		0.06687
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.34 (0.23, 0.45)	4, 0.18 (0.08, 0.31)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.14 (0.05, 0.28)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.APS.KM.S7.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	34 (46.6)	36 (46.2)
	Median Survival Est. (95% CI)	1.51 (0.79, 5.32)	1.08 (0.56, 1.77)
	Hazard Ratio (95% CI)		0.850 (0.532, 1.359)
	Treatment P-value [a]		0.45080
	Interaction P-value [b]		0.06687
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.35 (0.20, 0.50)	4, 0.29 (0.16, 0.43)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.29 (0.16, 0.43)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.APS.KM.S8.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	50 (51.0)	61 (57.0)
	Median Survival Est. (95% CI)	1.22 (0.76, 1.74)	0.99 (0.53, 1.71)
	Hazard Ratio (95% CI)		0.799 (0.550, 1.162)
	Treatment P-value [a]		0.23008
	Interaction P-value [b]		0.17397
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.34 (0.23, 0.46)	6, 0.21 (0.11, 0.33)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.APS.KM.S8.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	114 (56.2)	81 (40.5)
	Median Survival Est. (95% CI)	1.05 (0.76, 1.61)	1.41 (0.99, 1.91)
	Hazard Ratio (95% CI)		1.107 (0.833, 1.473)
	Treatment P-value [a]		0.45695
	Interaction P-value [b]		0.17397
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.29 (0.21, 0.37)	7, 0.31 (0.21, 0.42)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	2, 0.31 (0.21, 0.42)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.APS.KM.S9.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	142 (54.2)	126 (46.7)
	Median Survival Est. (95% CI)	1.15 (0.82, 1.54)	1.05 (0.76, 1.64)
	Hazard Ratio (95% CI)		0.931 (0.732, 1.183)
	Treatment P-value [a]		0.56073
	Interaction P-value [b]		0.27002
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.31 (0.24, 0.38)	11, 0.26 (0.18, 0.34)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.23 (0.15, 0.32)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.APS.KM.S9.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	22 (56.4)	16 (43.2)
	Median Survival Est. (95% CI)	0.99 (0.56, 1.71)	2.37 (0.72, NC)
	Hazard Ratio (95% CI)		1.371 (0.719, 2.613)
	Treatment P-value [a]		0.32395
	Interaction P-value [b]		0.27002
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.29 (0.14, 0.46)	2, 0.40 (0.21, 0.59)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.40 (0.21, 0.59)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.APS.KM.S10.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	39 (63.9)	29 (58.0)
	Median Survival Est. (95% CI)	1.18 (0.56, 1.64)	1.02 (0.36, 2.40)
	Hazard Ratio (95% CI)		1.002 (0.620, 1.621)
	Treatment P-value [a]		0.87534
	Interaction P-value [b]		0.93989
6 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.25 (0.14, 0.38)	3, 0.25 (0.12, 0.41)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.APS.KM.S10.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	111 (53.6)	95 (44.2)
	Median Survival Est. (95% CI)	0.99 (0.79, 1.51)	1.18 (0.76, 1.77)
	Hazard Ratio (95% CI)		1.024 (0.778, 1.347)
	Treatment P-value [a]		0.86451
	Interaction P-value [b]		0.93989
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.29 (0.22, 0.37)	9, 0.28 (0.19, 0.38)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	2, 0.28 (0.19, 0.38)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

2.4.1.7 Obstipation

Astellas: 7465-CL-0301
Table EORTC10.COS.KM.S1.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	43 (39.8)	38 (34.2)
	Median Survival Est. (95% CI)	2.14 (1.12, NC)	2.69 (1.45, NC)
	Hazard Ratio (95% CI)		0.985 (0.637, 1.525)
	Treatment P-value [a]		0.87918
	Interaction P-value [b]		0.78643
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.50 (0.38, 0.60)	7, 0.44 (0.30, 0.57)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.33 (0.10, 0.59)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.COS.KM.S1.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	87 (45.1)	71 (36.2)
	Median Survival Est. (95% CI)	1.94 (1.28, 5.39)	2.56 (1.22, NC)
	Hazard Ratio (95% CI)		1.061 (0.775, 1.454)
	Treatment P-value [a]		0.73667
	Interaction P-value [b]		0.78643
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.37 (0.28, 0.46)	10, 0.43 (0.33, 0.53)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.30 (0.20, 0.42)	2, 0.43 (0.33, 0.53)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.30 (0.20, 0.42)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.COS.KM.S2.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	107 (43.0)	83 (34.7)
	Median Survival Est. (95% CI)	2.14 (1.28, 9.99)	3.78 (1.25, NC)
	Hazard Ratio (95% CI)		1.005 (0.753, 1.340)
	Treatment P-value [a]		0.94701
	Interaction P-value [b]		0.58427
6 Months	Patients at Risk, Survival Est. (95% CI)	23, 0.42 (0.34, 0.50)	14, 0.46 (0.37, 0.54)
12 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.36 (0.24, 0.49)	0
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.36 (0.24, 0.49)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.COS.KM.S2.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	23 (44.2)	26 (38.2)
	Median Survival Est. (95% CI)	2.14 (1.05, 8.08)	2.56 (1.22, NC)
	Hazard Ratio (95% CI)		1.198 (0.683, 2.101)
	Treatment P-value [a]		0.58383
	Interaction P-value [b]		0.58427
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.33 (0.13, 0.55)	3, 0.37 (0.19, 0.55)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	2, 0.37 (0.19, 0.55)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.COS.KM.S3.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	101 (42.4)	83 (35.8)
	Median Survival Est. (95% CI)	2.14 (1.25, 8.08)	2.14 (1.25, NC)
	Hazard Ratio (95% CI)		0.992 (0.741, 1.327)
	Treatment P-value [a]		0.97939
	Interaction P-value [b]		0.55388
6 Months	Patients at Risk, Survival Est. (95% CI)	22, 0.42 (0.33, 0.50)	12, 0.44 (0.35, 0.52)
12 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.36 (0.26, 0.46)	1, 0.44 (0.35, 0.52)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.36 (0.26, 0.46)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.COS.KM.S3.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	29 (46.0)	26 (34.7)
	Median Survival Est. (95% CI)	1.68 (0.99, NC)	3.91 (1.22, NC)
	Hazard Ratio (95% CI)		1.190 (0.701, 2.021)
	Treatment P-value [a]		0.54179
	Interaction P-value [b]		0.55388
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.38 (0.22, 0.54)	5, 0.43 (0.25, 0.59)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.32 (0.12, 0.54)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.COS.KM.S4.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	52 (41.3)	38 (29.5)
	Median Survival Est. (95% CI)	2.14 (1.18, 8.08)	4.34 (0.92, NC)
	Hazard Ratio (95% CI)		1.042 (0.686, 1.583)
	Treatment P-value [a]		0.82965
	Interaction P-value [b]		0.14558
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.39 (0.26, 0.51)	6, 0.48 (0.35, 0.60)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.48 (0.35, 0.60)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.COS.KM.S4.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	11 (25.6)	17 (38.6)
	Median Survival Est. (95% CI)	5.55 (1.08, NC)	1.22 (0.82, NC)
	Hazard Ratio (95% CI)		0.519 (0.243, 1.110)
	Treatment P-value [a]		0.10118
	Interaction P-value [b]		0.14558
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.48 (0.22, 0.71)	1, 0.33 (0.15, 0.53)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.48 (0.22, 0.71)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.COS.KM.S4.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	67 (50.8)	54 (40.3)
	Median Survival Est. (95% CI)	1.45 (1.18, 8.08)	3.91 (1.64, NC)
	Hazard Ratio (95% CI)		1.204 (0.840, 1.726)
	Treatment P-value [a]		0.28603
	Interaction P-value [b]		0.14558
6 Months	Patients at Risk, Survival Est. (95% CI)	15, 0.41 (0.31, 0.50)	10, 0.43 (0.32, 0.55)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.36 (0.24, 0.48)	1, 0.43 (0.32, 0.55)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.36 (0.24, 0.48)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.COS.KM.S5.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	56 (46.7)	49 (39.5)
	Median Survival Est. (95% CI)	2.60 (1.18, NC)	3.78 (1.18, NC)
	Hazard Ratio (95% CI)		1.031 (0.701, 1.517)
	Treatment P-value [a]		0.87149
	Interaction P-value [b]		0.99451
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.46 (0.36, 0.56)	9, 0.44 (0.31, 0.56)
12 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.36 (0.20, 0.51)	1, 0.44 (0.31, 0.56)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.36 (0.20, 0.51)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.COS.KM.S5.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	74 (40.9)	60 (32.8)
	Median Survival Est. (95% CI)	2.14 (1.22, 5.52)	2.14 (1.25, NC)
	Hazard Ratio (95% CI)		1.033 (0.735, 1.453)
	Treatment P-value [a]		0.84369
	Interaction P-value [b]		0.99451
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.35 (0.25, 0.46)	8, 0.43 (0.31, 0.53)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.35 (0.20, 0.51)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.COS.KM.S6.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	33 (35.5)	32 (33.7)
	Median Survival Est. (95% CI)	3.29 (1.18, NC)	1.61 (1.18, NC)
	Hazard Ratio (95% CI)		0.798 (0.491, 1.299)
	Treatment P-value [a]		0.42186
	Interaction P-value [b]		0.22301
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.48 (0.35, 0.61)	1, 0.37 (0.22, 0.52)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.37 (0.22, 0.52)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.COS.KM.S6.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	97 (46.6)	77 (36.3)
	Median Survival Est. (95% CI)	1.94 (1.22, 5.52)	4.34 (1.64, NC)
	Hazard Ratio (95% CI)		1.139 (0.844, 1.538)
	Treatment P-value [a]		0.39362
	Interaction P-value [b]		0.22301
6 Months	Patients at Risk, Survival Est. (95% CI)	16, 0.38 (0.29, 0.47)	16, 0.46 (0.36, 0.55)
12 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.32 (0.22, 0.43)	1, 0.41 (0.29, 0.53)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.32 (0.22, 0.43)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.COS.KM.S7.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	66 (46.8)	38 (33.9)
	Median Survival Est. (95% CI)	1.38 (1.08, 3.81)	3.78 (1.64, NC)
	Hazard Ratio (95% CI)		1.279 (0.858, 1.908)
	Treatment P-value [a]		0.20757
	Interaction P-value [b]		0.29422
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.35 (0.25, 0.46)	3, 0.42 (0.25, 0.57)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.35 (0.25, 0.46)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.COS.KM.S7.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	35 (40.2)	41 (35.0)
	Median Survival Est. (95% CI)	5.52 (1.25, NC)	3.91 (1.18, NC)
	Hazard Ratio (95% CI)		0.936 (0.594, 1.475)
	Treatment P-value [a]		0.78547
	Interaction P-value [b]		0.29422
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.43 (0.28, 0.57)	9, 0.46 (0.33, 0.58)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.37 (0.20, 0.53)	1, 0.46 (0.33, 0.58)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.37 (0.20, 0.53)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.COS.KM.S7.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	29 (39.7)	30 (38.5)
	Median Survival Est. (95% CI)	2.43 (1.18, NC)	1.48 (0.72, NC)
	Hazard Ratio (95% CI)		0.778 (0.467, 1.297)
	Treatment P-value [a]		0.35254
	Interaction P-value [b]		0.29422
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.50 (0.36, 0.63)	5, 0.40 (0.25, 0.54)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.40 (0.25, 0.54)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.COS.KM.S8.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	43 (43.9)	49 (45.8)
	Median Survival Est. (95% CI)	1.54 (1.08, NC)	1.25 (0.99, 5.36)
	Hazard Ratio (95% CI)		0.874 (0.580, 1.316)
	Treatment P-value [a]		0.52925
	Interaction P-value [b]		0.26893
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.39 (0.26, 0.51)	3, 0.33 (0.19, 0.48)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.19 (0.02, 0.50)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.COS.KM.S8.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	87 (42.9)	60 (30.0)
	Median Survival Est. (95% CI)	2.60 (1.31, 8.08)	4.67 (1.74, NC)
	Hazard Ratio (95% CI)		1.175 (0.845, 1.635)
	Treatment P-value [a]		0.32099
	Interaction P-value [b]		0.26893
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.42 (0.33, 0.51)	14, 0.49 (0.39, 0.59)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.35 (0.24, 0.47)	2, 0.44 (0.30, 0.57)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.35 (0.24, 0.47)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.COS.KM.S9.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	115 (43.9)	96 (35.6)
	Median Survival Est. (95% CI)	2.10 (1.22, 5.39)	2.56 (1.48, 8.11)
	Hazard Ratio (95% CI)		1.040 (0.793, 1.364)
	Treatment P-value [a]		0.80093
	Interaction P-value [b]		0.89216
6 Months	Patients at Risk, Survival Est. (95% CI)	23, 0.39 (0.31, 0.47)	14, 0.42 (0.33, 0.50)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.29 (0.17, 0.42)	1, 0.37 (0.26, 0.48)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.COS.KM.S9.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	15 (38.5)	13 (35.1)
	Median Survival Est. (95% CI)	19.12 (1.08, NC)	NC (0.79, NC)
	Hazard Ratio (95% CI)		0.984 (0.462, 2.094)
	Treatment P-value [a]		0.98043
	Interaction P-value [b]		0.89216
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.54 (0.34, 0.69)	3, 0.56 (0.36, 0.71)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.54 (0.34, 0.69)	1, 0.56 (0.36, 0.71)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.54 (0.34, 0.69)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.COS.KM.S10.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	35 (57.4)	17 (34.0)
	Median Survival Est. (95% CI)	1.22 (0.99, 5.39)	NC (1.48, NC)
	Hazard Ratio (95% CI)		1.673 (0.937, 2.987)
	Treatment P-value [a]		0.08317
	Interaction P-value [b]		0.08013
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.34 (0.20, 0.48)	3, 0.56 (0.38, 0.70)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.COS.KM.S10.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	85 (41.1)	78 (36.3)
	Median Survival Est. (95% CI)	2.14 (1.38, 8.08)	1.71 (1.22, NC)
	Hazard Ratio (95% CI)		0.931 (0.684, 1.267)
	Treatment P-value [a]		0.65928
	Interaction P-value [b]		0.08013
6 Months	Patients at Risk, Survival Est. (95% CI)	18, 0.42 (0.33, 0.51)	13, 0.40 (0.31, 0.50)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.30 (0.16, 0.47)	2, 0.40 (0.31, 0.50)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.30 (0.16, 0.47)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

2.4.1.8 Diarrhö

Astellas: 7465-CL-0301
Table EORTC10.DIS.KM.S1.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	43 (39.8)	38 (34.2)
	Median Survival Est. (95% CI)	7.56 (0.95, NC)	5.32 (1.25, NC)
	Hazard Ratio (95% CI)		1.031 (0.666, 1.595)
	Treatment P-value [a]		0.86862
	Interaction P-value [b]		0.96964
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.50 (0.39, 0.61)	10, 0.44 (0.30, 0.58)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.DIS.KM.S1.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	86 (44.6)	76 (38.8)
	Median Survival Est. (95% CI)	1.94 (1.45, 6.83)	2.23 (1.54, 7.69)
	Hazard Ratio (95% CI)		1.020 (0.749, 1.389)
	Treatment P-value [a]		0.89783
	Interaction P-value [b]		0.96964
6 Months	Patients at Risk, Survival Est. (95% CI)	18, 0.42 (0.34, 0.51)	11, 0.42 (0.32, 0.52)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.27 (0.15, 0.41)	2, 0.23 (0.08, 0.41)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.DIS.KM.S2.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	110 (44.2)	91 (38.1)
	Median Survival Est. (95% CI)	2.10 (1.22, 7.49)	1.87 (1.28, 5.36)
	Hazard Ratio (95% CI)		0.965 (0.731, 1.275)
	Treatment P-value [a]		0.77966
	Interaction P-value [b]		0.50562
6 Months	Patients at Risk, Survival Est. (95% CI)	25, 0.46 (0.38, 0.53)	16, 0.40 (0.31, 0.49)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.25 (0.12, 0.39)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.DIS.KM.S2.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	19 (36.5)	23 (33.8)
	Median Survival Est. (95% CI)	2.23 (0.76, NC)	7.69 (1.81, NC)
	Hazard Ratio (95% CI)		1.211 (0.660, 2.225)
	Treatment P-value [a]		0.52374
	Interaction P-value [b]		0.50562
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.44 (0.26, 0.60)	5, 0.53 (0.37, 0.67)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	2, 0.40 (0.16, 0.63)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.DIS.KM.S3.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	105 (44.1)	88 (37.9)
	Median Survival Est. (95% CI)	1.94 (0.99, 6.83)	2.60 (1.58, 8.08)
	Hazard Ratio (95% CI)		1.078 (0.812, 1.432)
	Treatment P-value [a]		0.60591
	Interaction P-value [b]		0.42869
6 Months	Patients at Risk, Survival Est. (95% CI)	23, 0.43 (0.36, 0.51)	16, 0.42 (0.33, 0.51)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.28 (0.16, 0.41)	1, 0.25 (0.11, 0.42)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.DIS.KM.S3.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	24 (38.1)	26 (34.7)
	Median Survival Est. (95% CI)	9.63 (1.12, NC)	4.50 (0.99, NC)
	Hazard Ratio (95% CI)		0.838 (0.481, 1.461)
	Treatment P-value [a]		0.52189
	Interaction P-value [b]		0.42869
6 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.52 (0.37, 0.66)	5, 0.46 (0.30, 0.62)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.35 (0.14, 0.57)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.DIS.KM.S4.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	53 (42.1)	31 (24.0)
	Median Survival Est. (95% CI)	1.94 (0.79, 8.18)	NC (2.00, NC)
	Hazard Ratio (95% CI)		1.744 (1.119, 2.719)
	Treatment P-value [a]		0.01320
	Interaction P-value [b]		0.00306
6 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.43 (0.31, 0.54)	11, 0.59 (0.47, 0.70)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.51 (0.32, 0.67)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.DIS.KM.S4.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	13 (30.2)	22 (50.0)
	Median Survival Est. (95% CI)	2.40 (1.45, NC)	1.02 (0.62, 1.58)
	Hazard Ratio (95% CI)		0.449 (0.226, 0.893)
	Treatment P-value [a]		0.01255
	Interaction P-value [b]		0.00306
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.44 (0.22, 0.63)	1, 0.09 (0.01, 0.31)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.DIS.KM.S4.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	63 (47.7)	61 (45.5)
	Median Survival Est. (95% CI)	1.97 (1.02, 9.63)	2.60 (1.22, 8.08)
	Hazard Ratio (95% CI)		0.889 (0.624, 1.265)
	Treatment P-value [a]		0.50326
	Interaction P-value [b]		0.00306
6 Months	Patients at Risk, Survival Est. (95% CI)	18, 0.47 (0.37, 0.56)	9, 0.40 (0.28, 0.51)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.33 (0.19, 0.49)	1, 0.15 (0.01, 0.43)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.DIS.KM.S5.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	54 (45.0)	56 (45.2)
	Median Survival Est. (95% CI)	2.92 (1.45, NC)	2.17 (1.28, 8.08)
	Hazard Ratio (95% CI)		0.852 (0.586, 1.238)
	Treatment P-value [a]		0.40071
	Interaction P-value [b]		0.19094
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.49 (0.39, 0.59)	10, 0.39 (0.27, 0.50)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.32 (0.16, 0.50)	1, 0.22 (0.06, 0.43)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.DIS.KM.S5.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	75 (41.4)	58 (31.7)
	Median Survival Est. (95% CI)	1.84 (0.99, 6.83)	5.36 (1.54, NC)
	Hazard Ratio (95% CI)		1.195 (0.848, 1.684)
	Treatment P-value [a]		0.32680
	Interaction P-value [b]		0.19094
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.42 (0.33, 0.51)	11, 0.47 (0.36, 0.58)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.26 (0.12, 0.43)	1, 0.32 (0.14, 0.51)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Astellas: 7465-CL-0301
Table EORTC10.DIS.KM.S6.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	37 (39.8)	30 (31.6)
	Median Survival Est. (95% CI)	1.74 (0.76, NC)	2.00 (1.02, NC)
	Hazard Ratio (95% CI)		1.106 (0.683, 1.792)
	Treatment P-value [a]		0.61249
	Interaction P-value [b]		0.71039
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.41 (0.28, 0.53)	3, 0.49 (0.35, 0.61)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.25 (0.02, 0.60)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.DIS.KM.S6.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	92 (44.2)	84 (39.6)
	Median Survival Est. (95% CI)	2.17 (1.45, 8.18)	2.79 (1.61, 8.08)
	Hazard Ratio (95% CI)		0.994 (0.739, 1.336)
	Treatment P-value [a]		0.95967
	Interaction P-value [b]		0.71039
6 Months	Patients at Risk, Survival Est. (95% CI)	21, 0.47 (0.39, 0.55)	18, 0.42 (0.33, 0.51)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.28 (0.15, 0.43)	1, 0.27 (0.13, 0.43)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.DIS.KM.S7.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	66 (46.8)	35 (31.3)
	Median Survival Est. (95% CI)	1.84 (0.95, 7.49)	7.69 (1.87, NC)
	Hazard Ratio (95% CI)		1.426 (0.945, 2.150)
	Treatment P-value [a]		0.09146
	Interaction P-value [b]		0.00019
6 Months	Patients at Risk, Survival Est. (95% CI)	14, 0.41 (0.32, 0.51)	8, 0.51 (0.37, 0.64)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.28 (0.14, 0.43)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.DIS.KM.S7.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	34 (39.1)	60 (51.3)
	Median Survival Est. (95% CI)	2.23 (1.74, NC)	0.99 (0.59, 1.68)
	Hazard Ratio (95% CI)		0.509 (0.334, 0.776)
	Treatment P-value [a]		0.00201
	Interaction P-value [b]		0.00019
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.47 (0.34, 0.59)	3, 0.21 (0.10, 0.35)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.11 (0.01, 0.32)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.DIS.KM.S7.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	29 (39.7)	19 (24.4)
	Median Survival Est. (95% CI)	6.83 (0.79, 9.33)	NC (2.17, NC)
	Hazard Ratio (95% CI)		1.867 (1.046, 3.332)
	Treatment P-value [a]		0.02605
	Interaction P-value [b]		0.00019
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.52 (0.38, 0.64)	10, 0.64 (0.48, 0.76)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.53 (0.29, 0.72)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.DIS.KM.S8.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	42 (42.9)	44 (41.1)
	Median Survival Est. (95% CI)	1.77 (0.99, NC)	4.50 (1.71, 8.08)
	Hazard Ratio (95% CI)		1.108 (0.726, 1.692)
	Treatment P-value [a]		0.60888
	Interaction P-value [b]		0.62977
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.43 (0.31, 0.54)	9, 0.44 (0.31, 0.56)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.37 (0.23, 0.51)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.DIS.KM.S8.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	87 (42.9)	70 (35.0)
	Median Survival Est. (95% CI)	2.23 (1.02, 8.18)	1.81 (1.28, NC)
	Hazard Ratio (95% CI)		0.973 (0.710, 1.334)
	Treatment P-value [a]		0.86657
	Interaction P-value [b]		0.62977
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.47 (0.38, 0.55)	12, 0.43 (0.32, 0.52)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.26 (0.13, 0.41)	2, 0.35 (0.21, 0.50)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.DIS.KM.S9.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	111 (42.4)	99 (36.7)
	Median Survival Est. (95% CI)	2.14 (1.45, 7.56)	2.79 (1.54, 7.69)
	Hazard Ratio (95% CI)		0.997 (0.760, 1.308)
	Treatment P-value [a]		0.94588
	Interaction P-value [b]		0.59978
6 Months	Patients at Risk, Survival Est. (95% CI)	27, 0.46 (0.39, 0.53)	19, 0.43 (0.35, 0.52)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.30 (0.18, 0.42)	1, 0.23 (0.09, 0.41)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.DIS.KM.S9.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	18 (46.2)	15 (40.5)
	Median Survival Est. (95% CI)	2.10 (0.72, NC)	3.25 (1.02, NC)
	Hazard Ratio (95% CI)		1.215 (0.611, 2.413)
	Treatment P-value [a]		0.60859
	Interaction P-value [b]		0.59978
6 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.38 (0.20, 0.57)	2, 0.41 (0.18, 0.62)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.41 (0.18, 0.62)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.DIS.KM.S10.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	31 (50.8)	15 (30.0)
	Median Survival Est. (95% CI)	1.51 (0.82, NC)	8.77 (5.32, NC)
	Hazard Ratio (95% CI)		1.770 (0.955, 3.280)
	Treatment P-value [a]		0.07135
	Interaction P-value [b]		0.08761
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.39 (0.25, 0.53)	7, 0.56 (0.34, 0.74)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.39 (0.25, 0.53)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.DIS.KM.S10.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	86 (41.5)	81 (37.7)
	Median Survival Est. (95% CI)	2.20 (1.12, 7.56)	2.14 (1.28, 7.69)
	Hazard Ratio (95% CI)		0.972 (0.717, 1.317)
	Treatment P-value [a]		0.87528
	Interaction P-value [b]		0.08761
6 Months	Patients at Risk, Survival Est. (95% CI)	21, 0.46 (0.38, 0.54)	12, 0.42 (0.33, 0.51)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.23 (0.11, 0.39)	2, 0.33 (0.20, 0.46)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

2.4.1.9 Finanzielle Schwierigkeiten

Astellas: 7465-CL-0301
Table EORTC10.FIS.KM.S1.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	33 (30.6)	23 (20.7)
	Median Survival Est. (95% CI)	8.38 (5.36, NC)	NC (5.32, NC)
	Hazard Ratio (95% CI)		1.336 (0.784, 2.275)
	Treatment P-value [a]		0.29405
	Interaction P-value [b]		0.15628
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.62 (0.49, 0.72)	11, 0.63 (0.48, 0.75)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.43 (0.22, 0.62)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.FIS.KM.S1.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	48 (24.9)	49 (25.0)
	Median Survival Est. (95% CI)	NC (8.15, NC)	9.00 (5.42, NC)
	Hazard Ratio (95% CI)		0.826 (0.554, 1.230)
	Treatment P-value [a]		0.34220
	Interaction P-value [b]		0.15628
6 Months	Patients at Risk, Survival Est. (95% CI)	23, 0.66 (0.57, 0.74)	13, 0.59 (0.48, 0.69)
12 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.54 (0.38, 0.67)	3, 0.49 (0.29, 0.67)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.FIS.KM.S2.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	71 (28.5)	54 (22.6)
	Median Survival Est. (95% CI)	9.36 (7.56, NC)	NC (9.00, NC)
	Hazard Ratio (95% CI)		1.030 (0.723, 1.468)
	Treatment P-value [a]		0.89440
	Interaction P-value [b]		0.48095
6 Months	Patients at Risk, Survival Est. (95% CI)	32, 0.64 (0.55, 0.71)	18, 0.61 (0.50, 0.70)
12 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.46 (0.33, 0.59)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.FIS.KM.S2.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	10 (19.2)	18 (26.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (2.69, NC)
	Hazard Ratio (95% CI)		0.759 (0.350, 1.644)
	Treatment P-value [a]		0.44158
	Interaction P-value [b]		0.48095
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.71 (0.53, 0.84)	6, 0.60 (0.44, 0.73)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.71 (0.53, 0.84)	3, 0.60 (0.44, 0.73)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.FIS.KM.S3.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	66 (27.7)	56 (24.1)
	Median Survival Est. (95% CI)	NC (6.34, NC)	NC (5.42, NC)
	Hazard Ratio (95% CI)		0.991 (0.694, 1.416)
	Treatment P-value [a]		0.93576
	Interaction P-value [b]		0.86393
6 Months	Patients at Risk, Survival Est. (95% CI)	29, 0.62 (0.54, 0.70)	18, 0.60 (0.50, 0.69)
12 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.52 (0.39, 0.63)	2, 0.53 (0.37, 0.67)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.FIS.KM.S3.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	15 (23.8)	16 (21.3)
	Median Survival Est. (95% CI)	9.36 (8.15, NC)	NC (2.79, NC)
	Hazard Ratio (95% CI)		0.925 (0.457, 1.872)
	Treatment P-value [a]		0.84494
	Interaction P-value [b]		0.86393
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.72 (0.57, 0.83)	6, 0.62 (0.44, 0.76)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.62 (0.44, 0.76)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.FIS.KM.S4.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	24 (19.0)	22 (17.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI)		0.905 (0.507, 1.614)
	Treatment P-value [a]		0.71948
	Interaction P-value [b]		0.92789
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.73 (0.62, 0.81)	10, 0.68 (0.55, 0.78)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	2, 0.68 (0.55, 0.78)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.FIS.KM.S4.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	8 (18.6)	7 (15.9)
	Median Survival Est. (95% CI)	NC (5.45, NC)	NC (2.69, NC)
	Hazard Ratio (95% CI)		0.975 (0.353, 2.692)
	Treatment P-value [a]		0.99989
	Interaction P-value [b]		0.92789
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.68 (0.44, 0.83)	4, 0.70 (0.45, 0.85)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.68 (0.44, 0.83)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.FIS.KM.S4.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	49 (37.1)	43 (32.1)
	Median Survival Est. (95% CI)	8.15 (5.36, NC)	9.00 (3.98, NC)
	Hazard Ratio (95% CI)		1.041 (0.691, 1.568)
	Treatment P-value [a]		0.93680
	Interaction P-value [b]		0.92789
6 Months	Patients at Risk, Survival Est. (95% CI)	16, 0.59 (0.48, 0.68)	10, 0.54 (0.41, 0.65)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.34 (0.17, 0.52)	1, 0.36 (0.10, 0.63)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.FIS.KM.S5.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	33 (27.5)	27 (21.8)
	Median Survival Est. (95% CI)	NC (7.56, NC)	NC (NC , NC)
	Hazard Ratio (95% CI)		1.119 (0.673, 1.862)
	Treatment P-value [a]		0.63571
	Interaction P-value [b]		0.50014
6 Months	Patients at Risk, Survival Est. (95% CI)	19, 0.67 (0.55, 0.76)	11, 0.68 (0.57, 0.78)
12 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.57 (0.39, 0.71)	1, 0.68 (0.57, 0.78)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.FIS.KM.S5.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	48 (26.5)	45 (24.6)
	Median Survival Est. (95% CI)	8.38 (6.21, NC)	9.00 (2.69, NC)
	Hazard Ratio (95% CI)		0.894 (0.595, 1.344)
	Treatment P-value [a]		0.60304
	Interaction P-value [b]		0.50014
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.63 (0.53, 0.71)	13, 0.54 (0.42, 0.65)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.43 (0.25, 0.60)	2, 0.47 (0.31, 0.62)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.FIS.KM.S6.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	33 (35.5)	17 (17.9)
	Median Survival Est. (95% CI)	2.40 (1.31, NC)	NC (5.32, NC)
	Hazard Ratio (95% CI)		1.840 (1.024, 3.306)
	Treatment P-value [a]		0.03371
	Interaction P-value [b]		0.01109
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.50 (0.36, 0.62)	4, 0.64 (0.45, 0.77)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.34 (0.15, 0.54)	2, 0.64 (0.45, 0.77)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.FIS.KM.S6.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	48 (23.1)	55 (25.9)
	Median Survival Est. (95% CI)	NC (8.15, NC)	NC (5.42, NC)
	Hazard Ratio (95% CI)		0.741 (0.503, 1.091)
	Treatment P-value [a]		0.12578
	Interaction P-value [b]		0.01109
6 Months	Patients at Risk, Survival Est. (95% CI)	29, 0.70 (0.62, 0.77)	20, 0.60 (0.50, 0.68)
12 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.56 (0.41, 0.69)	1, 0.53 (0.37, 0.67)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.FIS.KM.S7.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	49 (34.8)	24 (21.4)
	Median Survival Est. (95% CI)	8.15 (2.76, NC)	NC (NC , NC)
	Hazard Ratio (95% CI)		1.348 (0.826, 2.198)
	Treatment P-value [a]		0.23876
	Interaction P-value [b]		0.16217
6 Months	Patients at Risk, Survival Est. (95% CI)	19, 0.58 (0.47, 0.67)	6, 0.65 (0.52, 0.76)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.38 (0.22, 0.53)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.FIS.KM.S7.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	20 (23.0)	30 (25.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	9.00 (5.32, NC)
	Hazard Ratio (95% CI)		0.742 (0.421, 1.308)
	Treatment P-value [a]		0.26909
	Interaction P-value [b]		0.16217
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.66 (0.51, 0.77)	10, 0.56 (0.40, 0.69)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.66 (0.51, 0.77)	1, 0.42 (0.17, 0.66)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.FIS.KM.S7.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	12 (16.4)	18 (23.1)
	Median Survival Est. (95% CI)	NC (6.21, NC)	NC (2.40, NC)
	Hazard Ratio (95% CI)		0.661 (0.318, 1.372)
	Treatment P-value [a]		0.24813
	Interaction P-value [b]		0.16217
6 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.78 (0.63, 0.87)	8, 0.62 (0.47, 0.75)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	2, 0.62 (0.47, 0.75)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.FIS.KM.S8.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	29 (29.6)	27 (25.2)
	Median Survival Est. (95% CI)	8.15 (6.21, NC)	NC (5.32, NC)
	Hazard Ratio (95% CI)		1.116 (0.660, 1.885)
	Treatment P-value [a]		0.71068
	Interaction P-value [b]		0.55199
6 Months	Patients at Risk, Survival Est. (95% CI)	15, 0.65 (0.51, 0.75)	11, 0.61 (0.47, 0.73)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.37 (0.17, 0.57)	1, 0.53 (0.32, 0.70)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.FIS.KM.S8.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	52 (25.6)	45 (22.5)
	Median Survival Est. (95% CI)	NC (8.38, NC)	NC (5.42, NC)
	Hazard Ratio (95% CI)		0.914 (0.613, 1.362)
	Treatment P-value [a]		0.70542
	Interaction P-value [b]		0.55199
6 Months	Patients at Risk, Survival Est. (95% CI)	21, 0.64 (0.55, 0.72)	13, 0.60 (0.49, 0.70)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.59 (0.45, 0.70)	2, 0.60 (0.49, 0.70)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.FIS.KM.S9.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	66 (25.2)	64 (23.7)
	Median Survival Est. (95% CI)	NC (8.15, NC)	NC (9.00, NC)
	Hazard Ratio (95% CI)		0.901 (0.638, 1.271)
	Treatment P-value [a]		0.54838
	Interaction P-value [b]		0.20580
6 Months	Patients at Risk, Survival Est. (95% CI)	32, 0.66 (0.58, 0.73)	22, 0.60 (0.50, 0.68)
12 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.52 (0.38, 0.64)	2, 0.53 (0.38, 0.66)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.FIS.KM.S9.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	15 (38.5)	8 (21.6)
	Median Survival Est. (95% CI)	6.34 (1.71, NC)	NC (2.69, NC)
	Hazard Ratio (95% CI)		1.636 (0.693, 3.861)
	Treatment P-value [a]		0.26245
	Interaction P-value [b]		0.20580
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.54 (0.34, 0.70)	2, 0.70 (0.46, 0.84)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.40 (0.15, 0.64)	1, 0.70 (0.46, 0.84)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.FIS.KM.S10.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	17 (27.9)	18 (36.0)
	Median Survival Est. (95% CI)	NC (8.15, NC)	2.66 (1.08, NC)
	Hazard Ratio (95% CI)		0.567 (0.292, 1.101)
	Treatment P-value [a]		0.07653
	Interaction P-value [b]		0.05656
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.67 (0.51, 0.79)	3, 0.48 (0.30, 0.65)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.50 (0.19, 0.75)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.FIS.KM.S10.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	59 (28.5)	47 (21.9)
	Median Survival Est. (95% CI)	8.38 (6.21, NC)	NC (9.00, NC)
	Hazard Ratio (95% CI)		1.195 (0.814, 1.754)
	Treatment P-value [a]		0.36109
	Interaction P-value [b]		0.05656
6 Months	Patients at Risk, Survival Est. (95% CI)	24, 0.61 (0.52, 0.69)	18, 0.63 (0.53, 0.72)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.49 (0.35, 0.61)	3, 0.56 (0.39, 0.70)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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2.4.2 Sensitivitätsanalyse (Responderschwelle ≥ 15 Punkte)

2.4.2.1 Fatigue

Astellas: 7465-CL-0301
Table EORTC15.FS.KM.S1.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	53 (49.1)	41 (36.9)
	Median Survival Est. (95% CI)	1.94 (0.95, 6.21)	2.37 (1.45, 7.69)
	Hazard Ratio (95% CI)		1.111 (0.739, 1.671)
	Treatment P-value [a]		0.55137
	Interaction P-value [b]		0.11732
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.39 (0.26, 0.51)	8, 0.42 (0.30, 0.54)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.FS.KM.S1.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	99 (51.3)	105 (53.6)
	Median Survival Est. (95% CI)	1.28 (0.99, 1.91)	1.02 (0.79, 1.28)
	Hazard Ratio (95% CI)		0.750 (0.570, 0.988)
	Treatment P-value [a]		0.04374
	Interaction P-value [b]		0.11732
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.30 (0.21, 0.39)	7, 0.17 (0.10, 0.26)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.25 (0.16, 0.35)	1, 0.17 (0.10, 0.26)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.FS.KM.S2.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	126 (50.6)	107 (44.8)
	Median Survival Est. (95% CI)	1.68 (1.22, 2.66)	1.41 (0.99, 2.00)
	Hazard Ratio (95% CI)		0.847 (0.655, 1.097)
	Treatment P-value [a]		0.22333
	Interaction P-value [b]		0.62341
6 Months	Patients at Risk, Survival Est. (95% CI)	19, 0.35 (0.27, 0.43)	11, 0.28 (0.20, 0.37)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.20 (0.11, 0.30)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.FS.KM.S2.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	26 (50.0)	39 (57.4)
	Median Survival Est. (95% CI)	0.79 (0.53, 5.32)	1.18 (0.79, 2.10)
	Hazard Ratio (95% CI)		0.975 (0.593, 1.602)
	Treatment P-value [a]		0.98961
	Interaction P-value [b]		0.62341
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.24 (0.09, 0.42)	4, 0.19 (0.09, 0.32)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.24 (0.09, 0.42)	1, 0.19 (0.09, 0.32)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Astellas: 7465-CL-0301
Table EORTC15.FS.KM.S3.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	125 (52.5)	113 (48.7)
	Median Survival Est. (95% CI)	1.28 (0.95, 1.94)	1.18 (0.95, 1.68)
	Hazard Ratio (95% CI)		0.855 (0.662, 1.103)
	Treatment P-value [a]		0.24567
	Interaction P-value [b]		0.84973
6 Months	Patients at Risk, Survival Est. (95% CI)	21, 0.33 (0.25, 0.41)	11, 0.24 (0.16, 0.33)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.21 (0.13, 0.30)	1, 0.18 (0.10, 0.29)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.FS.KM.S3.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	27 (42.9)	33 (44.0)
	Median Survival Est. (95% CI)	5.32 (1.22, 5.52)	1.68 (0.99, 4.14)
	Hazard Ratio (95% CI)		0.809 (0.486, 1.346)
	Treatment P-value [a]		0.34579
	Interaction P-value [b]		0.84973
6 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.29 (0.11, 0.49)	4, 0.28 (0.14, 0.43)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.FS.KM.S4.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	55 (43.7)	53 (41.1)
	Median Survival Est. (95% CI)	1.91 (0.95, 5.52)	0.99 (0.72, 1.41)
	Hazard Ratio (95% CI)		0.725 (0.497, 1.058)
	Treatment P-value [a]		0.10678
	Interaction P-value [b]		0.57956
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.37 (0.25, 0.50)	5, 0.27 (0.17, 0.39)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.FS.KM.S4.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	20 (46.5)	18 (40.9)
	Median Survival Est. (95% CI)	1.68 (0.76, 5.45)	1.12 (0.62, 2.66)
	Hazard Ratio (95% CI)		0.961 (0.508, 1.818)
	Treatment P-value [a]		0.90934
	Interaction P-value [b]		0.57956
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.23 (0.08, 0.42)	2, 0.31 (0.14, 0.49)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.23 (0.08, 0.42)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.FS.KM.S4.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	77 (58.3)	75 (56.0)
	Median Survival Est. (95% CI)	1.22 (0.89, 2.43)	1.68 (1.08, 2.46)
	Hazard Ratio (95% CI)		0.925 (0.673, 1.273)
	Treatment P-value [a]		0.55752
	Interaction P-value [b]		0.57956
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.34 (0.24, 0.44)	8, 0.24 (0.15, 0.35)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.19 (0.09, 0.31)	1, 0.14 (0.05, 0.28)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.FS.KM.S5.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	70 (58.3)	65 (52.4)
	Median Survival Est. (95% CI)	1.45 (0.85, 2.66)	1.61 (0.99, 2.37)
	Hazard Ratio (95% CI)		0.955 (0.681, 1.339)
	Treatment P-value [a]		0.69234
	Interaction P-value [b]		0.37562
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.29 (0.18, 0.40)	6, 0.27 (0.16, 0.39)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.17 (0.08, 0.30)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Table EORTC15.FS.KM.S5.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	82 (45.3)	81 (44.3)
	Median Survival Est. (95% CI)	1.68 (0.99, 5.42)	1.12 (0.76, 1.71)
	Hazard Ratio (95% CI)		0.777 (0.571, 1.056)
	Treatment P-value [a]		0.12014
	Interaction P-value [b]		0.37562
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.36 (0.27, 0.46)	9, 0.23 (0.14, 0.33)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.27 (0.16, 0.39)	1, 0.23 (0.14, 0.33)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.FS.KM.S6.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	44 (47.3)	42 (44.2)
	Median Survival Est. (95% CI)	1.48 (0.76, 5.42)	1.05 (0.72, 1.25)
	Hazard Ratio (95% CI)		0.721 (0.472, 1.103)
	Treatment P-value [a]		0.14768
	Interaction P-value [b]		0.37440
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.34 (0.21, 0.47)	2, 0.26 (0.15, 0.38)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.25 (0.13, 0.40)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.FS.KM.S6.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	108 (51.9)	104 (49.1)
	Median Survival Est. (95% CI)	1.64 (0.99, 2.43)	1.68 (0.99, 2.37)
	Hazard Ratio (95% CI)		0.906 (0.692, 1.186)
	Treatment P-value [a]		0.47581
	Interaction P-value [b]		0.37440
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.32 (0.24, 0.41)	13, 0.26 (0.18, 0.35)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.20 (0.10, 0.31)	1, 0.21 (0.12, 0.31)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.FS.KM.S7.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	74 (52.5)	50 (44.6)
	Median Survival Est. (95% CI)	1.25 (0.85, 2.43)	1.68 (1.05, 2.37)
	Hazard Ratio (95% CI)		0.986 (0.688, 1.412)
	Treatment P-value [a]		0.97606
	Interaction P-value [b]		0.62476
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.37 (0.27, 0.46)	5, 0.27 (0.16, 0.39)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.22 (0.11, 0.36)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.FS.KM.S7.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	45 (51.7)	59 (50.4)
	Median Survival Est. (95% CI)	1.68 (0.79, 5.45)	1.05 (0.72, 2.17)
	Hazard Ratio (95% CI)		0.780 (0.529, 1.151)
	Treatment P-value [a]		0.18572
	Interaction P-value [b]		0.62476
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.28 (0.16, 0.42)	6, 0.23 (0.12, 0.36)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.20 (0.09, 0.35)	1, 0.14 (0.04, 0.28)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.FS.KM.S7.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	33 (45.2)	37 (47.4)
	Median Survival Est. (95% CI)	1.54 (0.95, 5.52)	1.12 (0.72, 1.71)
	Hazard Ratio (95% CI)		0.785 (0.491, 1.255)
	Treatment P-value [a]		0.29372
	Interaction P-value [b]		0.62476
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.29 (0.13, 0.49)	4, 0.27 (0.14, 0.41)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.FS.KM.S8.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	50 (51.0)	62 (57.9)
	Median Survival Est. (95% CI)	1.45 (0.79, 5.42)	1.05 (0.95, 1.71)
	Hazard Ratio (95% CI)		0.809 (0.556, 1.175)
	Treatment P-value [a]		0.21364
	Interaction P-value [b]		0.67779
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.33 (0.21, 0.45)	3, 0.14 (0.05, 0.27)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.17 (0.06, 0.31)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.FS.KM.S8.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	102 (50.2)	84 (42.0)
	Median Survival Est. (95% CI)	1.68 (0.99, 2.66)	1.41 (0.82, 2.17)
	Hazard Ratio (95% CI)		0.894 (0.669, 1.193)
	Treatment P-value [a]		0.47413
	Interaction P-value [b]		0.67779
6 Months	Patients at Risk, Survival Est. (95% CI)	14, 0.33 (0.24, 0.42)	12, 0.32 (0.23, 0.41)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.25 (0.15, 0.36)	1, 0.28 (0.18, 0.39)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.FS.KM.S9.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	130 (49.6)	131 (48.5)
	Median Survival Est. (95% CI)	1.61 (1.12, 2.23)	1.18 (0.99, 1.68)
	Hazard Ratio (95% CI)		0.797 (0.625, 1.016)
	Treatment P-value [a]		0.06052
	Interaction P-value [b]		0.12438
6 Months	Patients at Risk, Survival Est. (95% CI)	21, 0.33 (0.26, 0.42)	11, 0.22 (0.15, 0.30)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.23 (0.15, 0.32)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.FS.KM.S9.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	22 (56.4)	15 (40.5)
	Median Survival Est. (95% CI)	0.99 (0.59, 5.49)	2.17 (0.76, NC)
	Hazard Ratio (95% CI)		1.380 (0.715, 2.661)
	Treatment P-value [a]		0.32204
	Interaction P-value [b]		0.12438
6 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.28 (0.12, 0.47)	4, 0.46 (0.26, 0.64)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.46 (0.26, 0.64)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.FS.KM.S10.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	35 (57.4)	31 (62.0)
	Median Survival Est. (95% CI)	1.61 (0.95, 5.32)	0.99 (0.53, 2.10)
	Hazard Ratio (95% CI)		0.712 (0.439, 1.155)
	Treatment P-value [a]		0.19612
	Interaction P-value [b]		0.34662
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.29 (0.15, 0.44)	4, 0.20 (0.08, 0.35)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.FS.KM.S10.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	102 (49.3)	98 (45.6)
	Median Survival Est. (95% CI)	1.28 (0.85, 1.97)	1.28 (1.02, 2.17)
	Hazard Ratio (95% CI)		0.931 (0.705, 1.229)
	Treatment P-value [a]		0.62677
	Interaction P-value [b]		0.34662
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.35 (0.27, 0.44)	9, 0.25 (0.16, 0.34)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.23 (0.14, 0.34)	1, 0.21 (0.12, 0.32)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

2.4.2.2 Übelkeit und Erbrechen

Astellas: 7465-CL-0301
Table EORTC15.NVS.KM.S1.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	51 (47.2)	47 (42.3)
	Median Survival Est. (95% CI)	1.64 (0.95, 5.36)	2.14 (0.76, 4.86)
	Hazard Ratio (95% CI)		0.944 (0.634, 1.404)
	Treatment P-value [a]		0.80770
	Interaction P-value [b]		0.44357
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.38 (0.27, 0.49)	10, 0.37 (0.25, 0.50)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.NVS.KM.S1.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	89 (46.1)	94 (48.0)
	Median Survival Est. (95% CI)	1.87 (1.25, 2.63)	1.28 (0.85, 1.74)
	Hazard Ratio (95% CI)		0.779 (0.583, 1.041)
	Treatment P-value [a]		0.09270
	Interaction P-value [b]		0.44357
6 Months	Patients at Risk, Survival Est. (95% CI)	14, 0.36 (0.27, 0.44)	8, 0.27 (0.18, 0.37)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.27 (0.18, 0.37)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.NVS.KM.S2.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	122 (49.0)	112 (46.9)
	Median Survival Est. (95% CI)	1.68 (1.22, 2.37)	1.18 (0.82, 1.71)
	Hazard Ratio (95% CI)		0.797 (0.616, 1.030)
	Treatment P-value [a]		0.09288
	Interaction P-value [b]		0.74610
6 Months	Patients at Risk, Survival Est. (95% CI)	19, 0.36 (0.28, 0.43)	13, 0.29 (0.21, 0.37)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.NVS.KM.S2.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	18 (34.6)	29 (42.6)
	Median Survival Est. (95% CI)	2.37 (0.82, NC)	1.97 (0.99, NC)
	Hazard Ratio (95% CI)		0.886 (0.492, 1.596)
	Treatment P-value [a]		0.64696
	Interaction P-value [b]		0.74610
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.42 (0.23, 0.60)	5, 0.37 (0.21, 0.52)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.37 (0.21, 0.52)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.NVS.KM.S3.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	113 (47.5)	103 (44.4)
	Median Survival Est. (95% CI)	1.61 (1.18, 2.14)	1.48 (0.85, 1.97)
	Hazard Ratio (95% CI)		0.893 (0.683, 1.167)
	Treatment P-value [a]		0.42764
	Interaction P-value [b]		0.28523
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.35 (0.28, 0.43)	13, 0.34 (0.25, 0.43)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.NVS.KM.S3.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	27 (42.9)	38 (50.7)
	Median Survival Est. (95% CI)	2.60 (1.51, NC)	1.05 (0.82, 1.87)
	Hazard Ratio (95% CI)		0.657 (0.401, 1.078)
	Treatment P-value [a]		0.06724
	Interaction P-value [b]		0.28523
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.41 (0.26, 0.56)	5, 0.23 (0.11, 0.37)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.23 (0.11, 0.37)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Astellas: 7465-CL-0301
Table EORTC15.NVS.KM.S4.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	52 (41.3)	45 (34.9)
	Median Survival Est. (95% CI)	1.74 (0.95, NC)	1.41 (0.95, NC)
	Hazard Ratio (95% CI)		0.908 (0.609, 1.354)
	Treatment P-value [a]		0.59716
	Interaction P-value [b]		0.77826
6 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.40 (0.29, 0.51)	4, 0.41 (0.29, 0.52)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.41 (0.29, 0.52)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Astellas: 7465-CL-0301
Table EORTC15.NVS.KM.S4.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	16 (37.2)	17 (38.6)
	Median Survival Est. (95% CI)	1.22 (0.56, NC)	0.85 (0.62, NC)
	Hazard Ratio (95% CI)		0.932 (0.470, 1.850)
	Treatment P-value [a]		0.94181
	Interaction P-value [b]		0.77826
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.41 (0.22, 0.58)	3, 0.38 (0.20, 0.57)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.NVS.KM.S4.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	72 (54.5)	79 (59.0)
	Median Survival Est. (95% CI)	1.84 (1.18, 2.63)	1.25 (0.76, 1.97)
	Hazard Ratio (95% CI)		0.772 (0.561, 1.062)
	Treatment P-value [a]		0.11311
	Interaction P-value [b]		0.77826
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.33 (0.24, 0.43)	11, 0.25 (0.16, 0.35)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.NVS.KM.S5.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	57 (47.5)	64 (51.6)
	Median Survival Est. (95% CI)	2.37 (1.22, NC)	1.45 (0.82, 1.97)
	Hazard Ratio (95% CI)		0.743 (0.520, 1.062)
	Treatment P-value [a]		0.09191
	Interaction P-value [b]		0.40044
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.43 (0.33, 0.53)	10, 0.30 (0.20, 0.42)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.15 (0.02, 0.41)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.NVS.KM.S5.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	83 (45.9)	77 (42.1)
	Median Survival Est. (95% CI)	1.68 (1.05, 2.30)	1.18 (0.82, 2.14)
	Hazard Ratio (95% CI)		0.910 (0.667, 1.241)
	Treatment P-value [a]		0.60194
	Interaction P-value [b]		0.40044
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.31 (0.22, 0.40)	8, 0.31 (0.21, 0.41)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.NVS.KM.S6.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	44 (47.3)	42 (44.2)
	Median Survival Est. (95% CI)	1.45 (0.59, 2.37)	0.76 (0.36, 1.22)
	Hazard Ratio (95% CI)		0.778 (0.509, 1.188)
	Treatment P-value [a]		0.19912
	Interaction P-value [b]		0.74504
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.29 (0.17, 0.41)	4, 0.29 (0.18, 0.42)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.15 (0.02, 0.40)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.NVS.KM.S6.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	96 (46.2)	99 (46.7)
	Median Survival Est. (95% CI)	2.14 (1.41, 3.58)	1.74 (1.15, 3.55)
	Hazard Ratio (95% CI)		0.846 (0.639, 1.121)
	Treatment P-value [a]		0.27141
	Interaction P-value [b]		0.74504
6 Months	Patients at Risk, Survival Est. (95% CI)	15, 0.40 (0.31, 0.48)	14, 0.31 (0.23, 0.41)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.NVS.KM.S7.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	75 (53.2)	51 (45.5)
	Median Survival Est. (95% CI)	1.51 (0.85, 2.37)	1.45 (0.85, 3.78)
	Hazard Ratio (95% CI)		0.996 (0.698, 1.422)
	Treatment P-value [a]		0.99722
	Interaction P-value [b]		0.07770
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.31 (0.22, 0.41)	6, 0.29 (0.18, 0.42)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.NVS.KM.S7.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	34 (39.1)	61 (52.1)
	Median Survival Est. (95% CI)	3.98 (1.41, NC)	0.99 (0.62, 1.87)
	Hazard Ratio (95% CI)		0.555 (0.365, 0.845)
	Treatment P-value [a]		0.00669
	Interaction P-value [b]		0.07770
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.46 (0.33, 0.58)	8, 0.26 (0.15, 0.37)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.NVS.KM.S7.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	31 (42.5)	29 (37.2)
	Median Survival Est. (95% CI)	1.68 (0.99, NC)	1.74 (0.99, NC)
	Hazard Ratio (95% CI)		1.012 (0.609, 1.680)
	Treatment P-value [a]		0.96254
	Interaction P-value [b]		0.07770
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.37 (0.22, 0.51)	4, 0.44 (0.30, 0.57)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.44 (0.30, 0.57)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.NVS.KM.S8.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	47 (48.0)	58 (54.2)
	Median Survival Est. (95% CI)	1.45 (1.12, 1.84)	1.15 (0.62, 1.97)
	Hazard Ratio (95% CI)		0.852 (0.580, 1.253)
	Treatment P-value [a]		0.46632
	Interaction P-value [b]		0.93091
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.36 (0.25, 0.47)	9, 0.31 (0.21, 0.43)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.NVS.KM.S8.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	93 (45.8)	83 (41.5)
	Median Survival Est. (95% CI)	2.14 (1.25, 3.58)	1.48 (0.99, 2.14)
	Hazard Ratio (95% CI)		0.834 (0.620, 1.122)
	Treatment P-value [a]		0.22349
	Interaction P-value [b]		0.93091
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.37 (0.28, 0.45)	9, 0.30 (0.20, 0.41)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.26 (0.16, 0.38)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Table EORTC15.NVS.KM.S9.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	121 (46.2)	126 (46.7)
	Median Survival Est. (95% CI)	1.84 (1.45, 2.60)	1.22 (0.99, 1.74)
	Hazard Ratio (95% CI)		0.791 (0.616, 1.016)
	Treatment P-value [a]		0.06548
	Interaction P-value [b]		0.26031
6 Months	Patients at Risk, Survival Est. (95% CI)	21, 0.37 (0.29, 0.44)	16, 0.30 (0.23, 0.38)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.09 (0.01, 0.29)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.NVS.KM.S9.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	19 (48.7)	15 (40.5)
	Median Survival Est. (95% CI)	1.41 (0.69, NC)	5.39 (0.39, NC)
	Hazard Ratio (95% CI)		1.198 (0.609, 2.358)
	Treatment P-value [a]		0.64190
	Interaction P-value [b]		0.26031
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.37 (0.20, 0.54)	2, 0.34 (0.09, 0.62)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.NVS.KM.S10.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	33 (54.1)	22 (44.0)
	Median Survival Est. (95% CI)	1.74 (1.22, 4.01)	1.91 (0.99, NC)
	Hazard Ratio (95% CI)		1.044 (0.609, 1.791)
	Treatment P-value [a]		0.82349
	Interaction P-value [b]		0.68524
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.34 (0.21, 0.48)	3, 0.41 (0.24, 0.57)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Astellas: 7465-CL-0301
Table EORTC15.NVS.KM.S10.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	100 (48.3)	98 (45.6)
	Median Survival Est. (95% CI)	1.25 (0.95, 1.87)	1.22 (0.82, 1.81)
	Hazard Ratio (95% CI)		0.921 (0.696, 1.218)
	Treatment P-value [a]		0.56450
	Interaction P-value [b]		0.68524
6 Months	Patients at Risk, Survival Est. (95% CI)	14, 0.33 (0.25, 0.41)	11, 0.27 (0.18, 0.37)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.14 (0.02, 0.38)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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2.4.2.3 Schmerz

Astellas: 7465-CL-0301
Table EORTC15.PS.KM.S1.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	60 (55.6)	53 (47.7)
	Median Survival Est. (95% CI)	0.99 (0.53, 2.14)	1.51 (0.99, 2.00)
	Hazard Ratio (95% CI)		1.048 (0.724, 1.518)
	Treatment P-value [a]		0.89863
	Interaction P-value [b]		0.17617
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.29 (0.17, 0.42)	5, 0.18 (0.08, 0.31)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.PS.KM.S1.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	105 (54.4)	106 (54.1)
	Median Survival Est. (95% CI)	1.25 (0.89, 1.64)	0.99 (0.56, 1.18)
	Hazard Ratio (95% CI)		0.764 (0.583, 1.002)
	Treatment P-value [a]		0.05970
	Interaction P-value [b]		0.17617
6 Months	Patients at Risk, Survival Est. (95% CI)	14, 0.29 (0.22, 0.37)	8, 0.19 (0.11, 0.27)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.25 (0.16, 0.34)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Astellas: 7465-CL-0301
Table EORTC15.PS.KM.S2.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	140 (56.2)	118 (49.4)
	Median Survival Est. (95% CI)	1.22 (0.89, 1.58)	1.18 (0.99, 1.61)
	Hazard Ratio (95% CI)		0.903 (0.706, 1.154)
	Treatment P-value [a]		0.40163
	Interaction P-value [b]		0.40849
6 Months	Patients at Risk, Survival Est. (95% CI)	18, 0.29 (0.22, 0.37)	10, 0.21 (0.13, 0.29)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.PS.KM.S2.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	25 (48.1)	41 (60.3)
	Median Survival Est. (95% CI)	1.05 (0.53, 3.68)	0.95 (0.43, 1.28)
	Hazard Ratio (95% CI)		0.714 (0.434, 1.175)
	Treatment P-value [a]		0.18852
	Interaction P-value [b]		0.40849
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.31 (0.16, 0.47)	3, 0.13 (0.05, 0.26)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.31 (0.16, 0.47)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.PS.KM.S3.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	135 (56.7)	120 (51.7)
	Median Survival Est. (95% CI)	1.02 (0.82, 1.48)	1.18 (0.95, 1.51)
	Hazard Ratio (95% CI)		0.907 (0.709, 1.160)
	Treatment P-value [a]		0.44362
	Interaction P-value [b]		0.29656
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.27 (0.20, 0.35)	10, 0.19 (0.12, 0.27)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.18 (0.11, 0.27)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.PS.KM.S3.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	30 (47.6)	39 (52.0)
	Median Survival Est. (95% CI)	1.48 (0.85, 9.99)	0.99 (0.79, 1.54)
	Hazard Ratio (95% CI)		0.681 (0.423, 1.098)
	Treatment P-value [a]		0.09507
	Interaction P-value [b]		0.29656
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.37 (0.22, 0.53)	3, 0.18 (0.08, 0.33)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.PS.KM.S4.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	60 (47.6)	58 (45.0)
	Median Survival Est. (95% CI)	1.05 (0.76, 2.14)	0.99 (0.43, 1.22)
	Hazard Ratio (95% CI)		0.738 (0.514, 1.060)
	Treatment P-value [a]		0.12427
	Interaction P-value [b]		0.54128
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.35 (0.23, 0.47)	5, 0.21 (0.12, 0.31)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.PS.KM.S4.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	20 (46.5)	18 (40.9)
	Median Survival Est. (95% CI)	1.58 (0.62, 3.68)	1.02 (0.76, 2.69)
	Hazard Ratio (95% CI)		0.831 (0.438, 1.575)
	Treatment P-value [a]		0.62359
	Interaction P-value [b]		0.54128
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.27 (0.11, 0.45)	1, 0.27 (0.11, 0.45)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.27 (0.11, 0.45)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.PS.KM.S4.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	85 (64.4)	83 (61.9)
	Median Survival Est. (95% CI)	1.02 (0.79, 1.48)	1.25 (0.95, 1.68)
	Hazard Ratio (95% CI)		0.963 (0.711, 1.303)
	Treatment P-value [a]		0.87477
	Interaction P-value [b]		0.54128
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.27 (0.19, 0.36)	7, 0.17 (0.09, 0.27)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.PS.KM.S5.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	70 (58.3)	72 (58.1)
	Median Survival Est. (95% CI)	1.45 (0.89, 2.14)	1.22 (0.85, 1.68)
	Hazard Ratio (95% CI)		0.843 (0.606, 1.172)
	Treatment P-value [a]		0.25136
	Interaction P-value [b]		0.91829
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.32 (0.21, 0.43)	5, 0.18 (0.09, 0.29)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.PS.KM.S5.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	95 (52.5)	87 (47.5)
	Median Survival Est. (95% CI)	1.02 (0.76, 1.48)	0.99 (0.72, 1.25)
	Hazard Ratio (95% CI)		0.863 (0.645, 1.154)
	Treatment P-value [a]		0.34841
	Interaction P-value [b]		0.91829
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.28 (0.20, 0.37)	8, 0.19 (0.11, 0.29)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.25 (0.17, 0.35)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Table EORTC15.PS.KM.S6.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	48 (51.6)	43 (45.3)
	Median Survival Est. (95% CI)	1.38 (0.82, 2.14)	0.99 (0.69, 1.38)
	Hazard Ratio (95% CI)		0.780 (0.516, 1.180)
	Treatment P-value [a]		0.26789
	Interaction P-value [b]		0.60611
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.30 (0.18, 0.42)	2, 0.18 (0.08, 0.32)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.17 (0.05, 0.36)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.PS.KM.S6.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	117 (56.3)	116 (54.7)
	Median Survival Est. (95% CI)	1.05 (0.82, 1.61)	1.18 (0.95, 1.61)
	Hazard Ratio (95% CI)		0.886 (0.686, 1.146)
	Treatment P-value [a]		0.38652
	Interaction P-value [b]		0.60611
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.29 (0.21, 0.37)	11, 0.19 (0.12, 0.27)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.PS.KM.S7.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	82 (58.2)	56 (50.0)
	Median Survival Est. (95% CI)	0.99 (0.79, 1.48)	1.18 (0.69, 1.68)
	Hazard Ratio (95% CI)		0.944 (0.672, 1.326)
	Treatment P-value [a]		0.75856
	Interaction P-value [b]		0.45954
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.30 (0.22, 0.39)	4, 0.20 (0.11, 0.32)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.PS.KM.S7.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	51 (58.6)	65 (55.6)
	Median Survival Est. (95% CI)	1.41 (0.59, 1.64)	1.02 (0.85, 1.51)
	Hazard Ratio (95% CI)		0.903 (0.625, 1.304)
	Treatment P-value [a]		0.52777
	Interaction P-value [b]		0.45954
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.22 (0.13, 0.34)	5, 0.15 (0.07, 0.27)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.18 (0.08, 0.31)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Astellas: 7465-CL-0301
Table EORTC15.PS.KM.S7.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	32 (43.8)	38 (48.7)
	Median Survival Est. (95% CI)	2.14 (0.85, 6.21)	1.15 (0.53, 1.51)
	Hazard Ratio (95% CI)		0.661 (0.413, 1.058)
	Treatment P-value [a]		0.10094
	Interaction P-value [b]		0.45954
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.37 (0.20, 0.54)	4, 0.23 (0.11, 0.36)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.PS.KM.S8.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	49 (50.0)	66 (61.7)
	Median Survival Est. (95% CI)	1.41 (0.82, 5.36)	0.99 (0.53, 1.25)
	Hazard Ratio (95% CI)		0.702 (0.484, 1.016)
	Treatment P-value [a]		0.06014
	Interaction P-value [b]		0.18482
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.36 (0.25, 0.48)	4, 0.16 (0.07, 0.27)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Astellas: 7465-CL-0301
Table EORTC15.PS.KM.S8.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	116 (57.1)	93 (46.5)
	Median Survival Est. (95% CI)	1.05 (0.82, 1.51)	1.22 (0.99, 1.54)
	Hazard Ratio (95% CI)		0.958 (0.729, 1.259)
	Treatment P-value [a]		0.82331
	Interaction P-value [b]		0.18482
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.26 (0.18, 0.35)	9, 0.21 (0.13, 0.30)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.21 (0.13, 0.31)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.PS.KM.S9.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	145 (55.3)	139 (51.5)
	Median Survival Est. (95% CI)	1.08 (0.89, 1.51)	1.08 (0.95, 1.28)
	Hazard Ratio (95% CI)		0.839 (0.665, 1.060)
	Treatment P-value [a]		0.14154
	Interaction P-value [b]		0.69561
6 Months	Patients at Risk, Survival Est. (95% CI)	18, 0.28 (0.21, 0.35)	11, 0.19 (0.13, 0.26)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.17 (0.08, 0.28)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.PS.KM.S9.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	20 (51.3)	20 (54.1)
	Median Survival Est. (95% CI)	1.45 (0.36, NC)	1.45 (0.72, 5.39)
	Hazard Ratio (95% CI)		0.958 (0.515, 1.782)
	Treatment P-value [a]		0.81413
	Interaction P-value [b]		0.69561
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.41 (0.24, 0.57)	2, 0.17 (0.04, 0.39)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.PS.KM.S10.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	39 (63.9)	34 (68.0)
	Median Survival Est. (95% CI)	1.22 (0.82, 1.71)	0.99 (0.36, 1.45)
	Hazard Ratio (95% CI)		0.743 (0.469, 1.177)
	Treatment P-value [a]		0.19900
	Interaction P-value [b]		0.25561
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.16 (0.04, 0.33)	2, 0.09 (0.02, 0.23)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.PS.KM.S10.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	112 (54.1)	101 (47.0)
	Median Survival Est. (95% CI)	0.99 (0.76, 1.48)	1.22 (1.02, 1.71)
	Hazard Ratio (95% CI)		1.013 (0.773, 1.326)
	Treatment P-value [a]		0.91083
	Interaction P-value [b]		0.25561
6 Months	Patients at Risk, Survival Est. (95% CI)	18, 0.31 (0.23, 0.39)	10, 0.24 (0.16, 0.33)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.17 (0.07, 0.31)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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2.4.2.4 Atemnot

Astellas: 7465-CL-0301
Table EORTC15.DS.KM.S1.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	42 (38.9)	39 (35.1)
	Median Survival Est. (95% CI)	5.45 (1.45, NC)	3.78 (1.71, 8.05)
	Hazard Ratio (95% CI)		0.936 (0.605, 1.448)
	Treatment P-value [a]		0.76028
	Interaction P-value [b]		0.27212
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.49 (0.36, 0.60)	10, 0.43 (0.30, 0.56)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.42 (0.26, 0.57)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.DS.KM.S1.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	76 (39.4)	91 (46.4)
	Median Survival Est. (95% CI)	3.58 (1.64, NC)	1.51 (1.18, 2.33)
	Hazard Ratio (95% CI)		0.695 (0.512, 0.943)
	Treatment P-value [a]		0.01726
	Interaction P-value [b]		0.27212
6 Months	Patients at Risk, Survival Est. (95% CI)	18, 0.46 (0.37, 0.55)	7, 0.27 (0.18, 0.37)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.40 (0.26, 0.53)	3, 0.27 (0.18, 0.37)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.DS.KM.S2.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	98 (39.4)	96 (40.2)
	Median Survival Est. (95% CI)	5.45 (1.71, NC)	2.33 (1.68, 3.78)
	Hazard Ratio (95% CI)		0.780 (0.588, 1.033)
	Treatment P-value [a]		0.08601
	Interaction P-value [b]		0.95375
6 Months	Patients at Risk, Survival Est. (95% CI)	27, 0.49 (0.41, 0.56)	13, 0.33 (0.24, 0.42)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.46 (0.37, 0.55)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.DS.KM.S2.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	20 (38.5)	34 (50.0)
	Median Survival Est. (95% CI)	2.60 (1.02, NC)	1.28 (0.99, 2.23)
	Hazard Ratio (95% CI)		0.765 (0.440, 1.330)
	Treatment P-value [a]		0.33048
	Interaction P-value [b]		0.95375
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.38 (0.19, 0.57)	4, 0.29 (0.16, 0.44)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.25 (0.06, 0.50)	3, 0.29 (0.16, 0.44)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.DS.KM.S3.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	95 (39.9)	103 (44.4)
	Median Survival Est. (95% CI)	4.44 (1.64, NC)	1.68 (1.22, 2.43)
	Hazard Ratio (95% CI)		0.726 (0.549, 0.959)
	Treatment P-value [a]		0.02205
	Interaction P-value [b]		0.48967
6 Months	Patients at Risk, Survival Est. (95% CI)	24, 0.47 (0.39, 0.55)	12, 0.30 (0.21, 0.39)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.39 (0.26, 0.51)	2, 0.23 (0.14, 0.34)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Table EORTC15.DS.KM.S3.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	23 (36.5)	27 (36.0)
	Median Survival Est. (95% CI)	3.58 (1.61, NC)	2.46 (1.68, NC)
	Hazard Ratio (95% CI)		0.903 (0.518, 1.576)
	Treatment P-value [a]		0.74169
	Interaction P-value [b]		0.48967
6 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.49 (0.33, 0.63)	5, 0.42 (0.26, 0.56)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.42 (0.26, 0.56)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.DS.KM.S4.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	40 (31.7)	50 (38.8)
	Median Survival Est. (95% CI)	NC (1.68, NC)	1.28 (0.79, 2.66)
	Hazard Ratio (95% CI)		0.568 (0.374, 0.861)
	Treatment P-value [a]		0.00997
	Interaction P-value [b]		0.20390
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.52 (0.39, 0.64)	6, 0.29 (0.17, 0.41)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	2, 0.29 (0.17, 0.41)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.DS.KM.S4.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	13 (30.2)	14 (31.8)
	Median Survival Est. (95% CI)	NC (0.82, NC)	2.60 (1.12, NC)
	Hazard Ratio (95% CI)		0.849 (0.398, 1.813)
	Treatment P-value [a]		0.86901
	Interaction P-value [b]		0.20390
6 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.51 (0.30, 0.68)	2, 0.37 (0.16, 0.58)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.51 (0.30, 0.68)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.DS.KM.S4.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	65 (49.2)	66 (49.3)
	Median Survival Est. (95% CI)	2.60 (1.61, 7.56)	2.33 (1.51, 4.37)
	Hazard Ratio (95% CI)		0.922 (0.654, 1.299)
	Treatment P-value [a]		0.63409
	Interaction P-value [b]		0.20390
6 Months	Patients at Risk, Survival Est. (95% CI)	16, 0.43 (0.33, 0.52)	9, 0.34 (0.24, 0.45)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.25 (0.08, 0.48)	1, 0.25 (0.13, 0.39)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.DS.KM.S5.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	42 (35.0)	58 (46.8)
	Median Survival Est. (95% CI)	NC (5.36, NC)	2.37 (1.61, 4.60)
	Hazard Ratio (95% CI)		0.625 (0.420, 0.930)
	Treatment P-value [a]		0.01437
	Interaction P-value [b]		0.19721
6 Months	Patients at Risk, Survival Est. (95% CI)	19, 0.57 (0.45, 0.67)	7, 0.35 (0.24, 0.47)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.53 (0.40, 0.64)	1, 0.25 (0.13, 0.40)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.DS.KM.S5.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	76 (42.0)	72 (39.3)
	Median Survival Est. (95% CI)	1.71 (1.28, 4.44)	1.71 (1.02, 2.66)
	Hazard Ratio (95% CI)		0.875 (0.634, 1.208)
	Treatment P-value [a]		0.40971
	Interaction P-value [b]		0.19721
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.40 (0.31, 0.49)	10, 0.30 (0.20, 0.41)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.32 (0.17, 0.48)	2, 0.30 (0.20, 0.41)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.DS.KM.S6.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	35 (37.6)	38 (40.0)
	Median Survival Est. (95% CI)	2.60 (1.38, NC)	1.51 (1.12, 2.66)
	Hazard Ratio (95% CI)		0.717 (0.453, 1.136)
	Treatment P-value [a]		0.16642
	Interaction P-value [b]		0.74224
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.45 (0.31, 0.58)	3, 0.25 (0.12, 0.40)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.45 (0.31, 0.58)	2, 0.25 (0.12, 0.40)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.DS.KM.S6.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	83 (39.9)	92 (43.4)
	Median Survival Est. (95% CI)	4.44 (1.71, NC)	2.23 (1.68, 4.17)
	Hazard Ratio (95% CI)		0.786 (0.584, 1.058)
	Treatment P-value [a]		0.11947
	Interaction P-value [b]		0.74224
6 Months	Patients at Risk, Survival Est. (95% CI)	21, 0.49 (0.40, 0.57)	14, 0.35 (0.26, 0.44)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.39 (0.25, 0.53)	1, 0.29 (0.19, 0.40)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.DS.KM.S7.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	63 (44.7)	45 (40.2)
	Median Survival Est. (95% CI)	2.66 (1.54, 7.56)	2.10 (1.48, 4.37)
	Hazard Ratio (95% CI)		0.922 (0.629, 1.352)
	Treatment P-value [a]		0.66552
	Interaction P-value [b]		0.20802
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.42 (0.31, 0.52)	7, 0.34 (0.21, 0.46)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.28 (0.12, 0.47)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.DS.KM.S7.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	35 (40.2)	51 (43.6)
	Median Survival Est. (95% CI)	2.46 (1.41, NC)	1.94 (1.25, 5.36)
	Hazard Ratio (95% CI)		0.787 (0.512, 1.211)
	Treatment P-value [a]		0.27620
	Interaction P-value [b]		0.20802
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.47 (0.35, 0.59)	6, 0.32 (0.19, 0.45)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.47 (0.35, 0.59)	1, 0.27 (0.13, 0.42)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.DS.KM.S7.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	20 (27.4)	34 (43.6)
	Median Survival Est. (95% CI)	NC (1.68, NC)	1.71 (0.79, 3.19)
	Hazard Ratio (95% CI)		0.503 (0.290, 0.874)
	Treatment P-value [a]		0.01430
	Interaction P-value [b]		0.20802
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.62 (0.47, 0.74)	4, 0.31 (0.18, 0.45)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	2, 0.31 (0.18, 0.45)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.DS.KM.S8.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	45 (45.9)	53 (49.5)
	Median Survival Est. (95% CI)	1.64 (1.02, 5.36)	1.68 (1.25, 2.46)
	Hazard Ratio (95% CI)		0.958 (0.644, 1.425)
	Treatment P-value [a]		0.86422
	Interaction P-value [b]		0.21595
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.37 (0.25, 0.48)	6, 0.28 (0.17, 0.41)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.27 (0.12, 0.46)	1, 0.24 (0.12, 0.38)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.DS.KM.S8.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	73 (36.0)	77 (38.5)
	Median Survival Est. (95% CI)	9.36 (2.63, NC)	2.23 (1.38, 4.17)
	Hazard Ratio (95% CI)		0.694 (0.504, 0.956)
	Treatment P-value [a]		0.02865
	Interaction P-value [b]		0.21595
6 Months	Patients at Risk, Survival Est. (95% CI)	21, 0.52 (0.43, 0.60)	11, 0.35 (0.26, 0.45)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.46 (0.31, 0.59)	2, 0.31 (0.20, 0.43)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.DS.KM.S9.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	100 (38.2)	110 (40.7)
	Median Survival Est. (95% CI)	5.36 (1.91, NC)	2.17 (1.48, 2.83)
	Hazard Ratio (95% CI)		0.761 (0.580, 0.998)
	Treatment P-value [a]		0.05157
	Interaction P-value [b]		0.84749
6 Months	Patients at Risk, Survival Est. (95% CI)	29, 0.49 (0.42, 0.56)	16, 0.34 (0.25, 0.42)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.42 (0.30, 0.53)	2, 0.28 (0.19, 0.38)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.DS.KM.S9.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	18 (46.2)	20 (54.1)
	Median Survival Est. (95% CI)	1.71 (0.82, NC)	1.94 (1.02, 4.60)
	Hazard Ratio (95% CI)		0.815 (0.430, 1.545)
	Treatment P-value [a]		0.52896
	Interaction P-value [b]		0.84749
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.36 (0.17, 0.56)	1, 0.25 (0.09, 0.45)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.25 (0.09, 0.45)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.DS.KM.S10.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	24 (39.3)	26 (52.0)
	Median Survival Est. (95% CI)	NC (1.64, NC)	1.68 (0.99, 7.46)
	Hazard Ratio (95% CI)		0.590 (0.339, 1.028)
	Treatment P-value [a]		0.06780
	Interaction P-value [b]		0.13424
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.52 (0.37, 0.65)	4, 0.35 (0.20, 0.51)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.DS.KM.S10.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	87 (42.0)	84 (39.1)
	Median Survival Est. (95% CI)	2.50 (1.45, 7.56)	2.43 (1.68, 4.37)
	Hazard Ratio (95% CI)		0.956 (0.708, 1.290)
	Treatment P-value [a]		0.72682
	Interaction P-value [b]		0.13424
6 Months	Patients at Risk, Survival Est. (95% CI)	20, 0.42 (0.33, 0.51)	11, 0.33 (0.23, 0.43)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.33 (0.20, 0.47)	3, 0.33 (0.23, 0.43)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

2.4.2.5 Schlaflosigkeit

Astellas: 7465-CL-0301
Table EORTC15.SLS.KM.S1.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	51 (47.2)	41 (36.9)
	Median Survival Est. (95% CI)	1.91 (0.76, 6.54)	2.46 (1.71, 7.46)
	Hazard Ratio (95% CI)		1.222 (0.810, 1.844)
	Treatment P-value [a]		0.35139
	Interaction P-value [b]		0.05953
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.38 (0.26, 0.51)	8, 0.38 (0.24, 0.52)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.SLS.KM.S1.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	88 (45.6)	93 (47.4)
	Median Survival Est. (95% CI)	1.68 (1.05, 5.52)	1.15 (0.82, 1.74)
	Hazard Ratio (95% CI)		0.752 (0.562, 1.008)
	Treatment P-value [a]		0.05980
	Interaction P-value [b]		0.05953
6 Months	Patients at Risk, Survival Est. (95% CI)	16, 0.35 (0.25, 0.45)	9, 0.29 (0.20, 0.39)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.30 (0.19, 0.41)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.SLS.KM.S2.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	120 (48.2)	96 (40.2)
	Median Survival Est. (95% CI)	1.81 (1.05, 2.60)	1.94 (1.18, 4.17)
	Hazard Ratio (95% CI)		1.017 (0.777, 1.330)
	Treatment P-value [a]		0.89903
	Interaction P-value [b]		0.05367
6 Months	Patients at Risk, Survival Est. (95% CI)	20, 0.36 (0.27, 0.44)	14, 0.36 (0.27, 0.46)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.25 (0.15, 0.37)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.SLS.KM.S2.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	19 (36.5)	38 (55.9)
	Median Survival Est. (95% CI)	2.23 (0.99, NC)	0.99 (0.56, 1.68)
	Hazard Ratio (95% CI)		0.556 (0.320, 0.965)
	Treatment P-value [a]		0.03722
	Interaction P-value [b]		0.05367
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.37 (0.15, 0.60)	3, 0.20 (0.09, 0.35)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.37 (0.15, 0.60)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.SLS.KM.S3.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	114 (47.9)	101 (43.5)
	Median Survival Est. (95% CI)	1.45 (0.99, 2.23)	1.45 (1.02, 2.37)
	Hazard Ratio (95% CI)		0.952 (0.728, 1.244)
	Treatment P-value [a]		0.73032
	Interaction P-value [b]		0.30174
6 Months	Patients at Risk, Survival Est. (95% CI)	19, 0.35 (0.27, 0.43)	14, 0.33 (0.24, 0.42)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.28 (0.19, 0.38)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.SLS.KM.S3.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	25 (39.7)	33 (44.0)
	Median Survival Est. (95% CI)	5.52 (1.15, NC)	1.77 (1.08, 2.46)
	Hazard Ratio (95% CI)		0.699 (0.416, 1.176)
	Treatment P-value [a]		0.15411
	Interaction P-value [b]		0.30174
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.38 (0.17, 0.59)	3, 0.29 (0.15, 0.45)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.SLS.KM.S4.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	49 (38.9)	54 (41.9)
	Median Survival Est. (95% CI)	2.40 (1.28, 9.07)	0.99 (0.39, 1.48)
	Hazard Ratio (95% CI)		0.577 (0.392, 0.850)
	Treatment P-value [a]		0.00594
	Interaction P-value [b]		0.01354
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.41 (0.27, 0.55)	4, 0.27 (0.17, 0.38)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.SLS.KM.S4.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	15 (34.9)	17 (38.6)
	Median Survival Est. (95% CI)	1.87 (1.05, NC)	1.74 (0.82, 7.69)
	Hazard Ratio (95% CI)		0.807 (0.403, 1.618)
	Treatment P-value [a]		0.60672
	Interaction P-value [b]		0.01354
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.43 (0.23, 0.61)	2, 0.37 (0.18, 0.55)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.43 (0.23, 0.61)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.SLS.KM.S4.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	75 (56.8)	63 (47.0)
	Median Survival Est. (95% CI)	1.05 (0.89, 2.60)	2.46 (1.25, 5.39)
	Hazard Ratio (95% CI)		1.239 (0.886, 1.733)
	Treatment P-value [a]		0.26483
	Interaction P-value [b]		0.01354
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.31 (0.21, 0.42)	11, 0.35 (0.23, 0.47)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.25 (0.15, 0.37)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.SLS.KM.S5.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	63 (52.5)	57 (46.0)
	Median Survival Est. (95% CI)	1.45 (0.99, 5.68)	2.33 (1.05, 5.45)
	Hazard Ratio (95% CI)		0.991 (0.692, 1.419)
	Treatment P-value [a]		0.84496
	Interaction P-value [b]		0.44503
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.37 (0.26, 0.49)	6, 0.34 (0.20, 0.48)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.24 (0.11, 0.40)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.SLS.KM.S5.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	76 (42.0)	77 (42.1)
	Median Survival Est. (95% CI)	1.91 (1.02, 5.52)	1.31 (0.99, 1.87)
	Hazard Ratio (95% CI)		0.822 (0.599, 1.129)
	Treatment P-value [a]		0.21142
	Interaction P-value [b]		0.44503
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.35 (0.24, 0.46)	11, 0.29 (0.20, 0.39)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.31 (0.19, 0.43)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.SLS.KM.S6.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	40 (43.0)	43 (45.3)
	Median Survival Est. (95% CI)	1.31 (0.99, 6.54)	0.99 (0.53, 1.22)
	Hazard Ratio (95% CI)		0.619 (0.402, 0.954)
	Treatment P-value [a]		0.02593
	Interaction P-value [b]		0.05921
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.37 (0.24, 0.51)	1, 0.13 (0.02, 0.37)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.22 (0.06, 0.43)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.SLS.KM.S6.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	99 (47.6)	91 (42.9)
	Median Survival Est. (95% CI)	1.87 (1.05, 5.42)	1.94 (1.25, 4.37)
	Hazard Ratio (95% CI)		1.019 (0.766, 1.354)
	Treatment P-value [a]		0.89753
	Interaction P-value [b]		0.05921
6 Months	Patients at Risk, Survival Est. (95% CI)	15, 0.35 (0.25, 0.45)	16, 0.37 (0.28, 0.46)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.29 (0.19, 0.40)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.SLS.KM.S7.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	70 (49.6)	42 (37.5)
	Median Survival Est. (95% CI)	1.08 (0.89, 2.60)	2.43 (1.02, 7.69)
	Hazard Ratio (95% CI)		1.136 (0.774, 1.667)
	Treatment P-value [a]		0.49503
	Interaction P-value [b]		0.14729
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.35 (0.24, 0.45)	5, 0.35 (0.19, 0.51)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.31 (0.20, 0.43)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.SLS.KM.S7.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	41 (47.1)	57 (48.7)
	Median Survival Est. (95% CI)	1.81 (0.99, 5.52)	1.71 (1.05, 2.46)
	Hazard Ratio (95% CI)		0.895 (0.599, 1.337)
	Treatment P-value [a]		0.55689
	Interaction P-value [b]		0.14729
6 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.34 (0.20, 0.49)	8, 0.29 (0.18, 0.41)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.29 (0.14, 0.45)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.SLS.KM.S7.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	28 (38.4)	35 (44.9)
	Median Survival Est. (95% CI)	5.42 (1.28, 9.07)	1.02 (0.53, 1.77)
	Hazard Ratio (95% CI)		0.607 (0.369, 0.998)
	Treatment P-value [a]		0.04774
	Interaction P-value [b]		0.14729
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.39 (0.20, 0.58)	4, 0.31 (0.19, 0.45)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.SLS.KM.S8.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	46 (46.9)	58 (54.2)
	Median Survival Est. (95% CI)	1.41 (0.85, 6.54)	1.08 (0.82, 1.74)
	Hazard Ratio (95% CI)		0.787 (0.534, 1.161)
	Treatment P-value [a]		0.21710
	Interaction P-value [b]		0.38359
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.38 (0.25, 0.50)	5, 0.25 (0.13, 0.39)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.23 (0.07, 0.44)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.SLS.KM.S8.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	93 (45.8)	76 (38.0)
	Median Survival Est. (95% CI)	1.91 (1.05, 5.42)	1.87 (1.18, 4.37)
	Hazard Ratio (95% CI)		0.980 (0.724, 1.328)
	Treatment P-value [a]		0.93695
	Interaction P-value [b]		0.38359
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.34 (0.24, 0.45)	12, 0.36 (0.26, 0.46)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.27 (0.16, 0.40)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.SLS.KM.S9.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	120 (45.8)	117 (43.3)
	Median Survival Est. (95% CI)	1.81 (1.05, 5.42)	1.31 (1.02, 2.37)
	Hazard Ratio (95% CI)		0.878 (0.681, 1.134)
	Treatment P-value [a]		0.31791
	Interaction P-value [b]		0.72072
6 Months	Patients at Risk, Survival Est. (95% CI)	21, 0.37 (0.28, 0.45)	15, 0.33 (0.25, 0.41)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.29 (0.18, 0.39)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.SLS.KM.S9.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	19 (48.7)	17 (45.9)
	Median Survival Est. (95% CI)	1.81 (0.99, 6.54)	1.94 (0.82, NC)
	Hazard Ratio (95% CI)		0.998 (0.519, 1.921)
	Treatment P-value [a]		0.89969
	Interaction P-value [b]		0.72072
6 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.32 (0.12, 0.55)	2, 0.27 (0.07, 0.53)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.SLS.KM.S10.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	38 (62.3)	24 (48.0)
	Median Survival Est. (95% CI)	1.02 (0.59, 1.68)	1.84 (0.99, 7.46)
	Hazard Ratio (95% CI)		1.402 (0.840, 2.340)
	Treatment P-value [a]		0.15625
	Interaction P-value [b]		0.05847
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.15 (0.02, 0.41)	5, 0.38 (0.23, 0.54)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.SLS.KM.S10.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	90 (43.5)	95 (44.2)
	Median Survival Est. (95% CI)	1.91 (1.05, 5.42)	1.22 (0.99, 2.37)
	Hazard Ratio (95% CI)		0.794 (0.595, 1.060)
	Treatment P-value [a]		0.12018
	Interaction P-value [b]		0.05847
6 Months	Patients at Risk, Survival Est. (95% CI)	19, 0.39 (0.30, 0.48)	10, 0.28 (0.19, 0.38)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.31 (0.19, 0.44)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

2.4.2.6 Appetitverlust

Astellas: 7465-CL-0301
Table EORTC15.APS.KM.S1.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	55 (50.9)	47 (42.3)
	Median Survival Est. (95% CI)	1.51 (0.79, 5.32)	1.05 (0.62, 5.32)
	Hazard Ratio (95% CI)		0.938 (0.636, 1.385)
	Treatment P-value [a]		0.69871
	Interaction P-value [b]		0.77857
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.38 (0.27, 0.49)	5, 0.30 (0.16, 0.45)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.APS.KM.S1.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	109 (56.5)	95 (48.5)
	Median Survival Est. (95% CI)	0.99 (0.76, 1.28)	1.18 (0.76, 1.71)
	Hazard Ratio (95% CI)		1.005 (0.763, 1.324)
	Treatment P-value [a]		0.90433
	Interaction P-value [b]		0.77857
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.27 (0.19, 0.35)	8, 0.26 (0.17, 0.35)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	2, 0.26 (0.17, 0.35)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.APS.KM.S2.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	137 (55.0)	104 (43.5)
	Median Survival Est. (95% CI)	1.25 (0.95, 1.64)	1.15 (0.79, 1.87)
	Hazard Ratio (95% CI)		0.967 (0.749, 1.249)
	Treatment P-value [a]		0.82394
	Interaction P-value [b]		0.55486
6 Months	Patients at Risk, Survival Est. (95% CI)	16, 0.31 (0.24, 0.39)	8, 0.30 (0.20, 0.40)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.APS.KM.S2.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	27 (51.9)	38 (55.9)
	Median Survival Est. (95% CI)	0.56 (0.49, 1.08)	1.08 (0.56, 1.77)
	Hazard Ratio (95% CI)		1.144 (0.698, 1.876)
	Treatment P-value [a]		0.65871
	Interaction P-value [b]		0.55486
6 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.30 (0.16, 0.44)	5, 0.22 (0.11, 0.35)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	2, 0.22 (0.11, 0.35)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.APS.KM.S3.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	136 (57.1)	102 (44.0)
	Median Survival Est. (95% CI)	0.99 (0.76, 1.28)	1.51 (0.99, 1.97)
	Hazard Ratio (95% CI)		1.129 (0.873, 1.460)
	Treatment P-value [a]		0.34647
	Interaction P-value [b]		0.02192
6 Months	Patients at Risk, Survival Est. (95% CI)	14, 0.28 (0.21, 0.35)	9, 0.30 (0.20, 0.39)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.26 (0.16, 0.37)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Table EORTC15.APS.KM.S3.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	28 (44.4)	40 (53.3)
	Median Survival Est. (95% CI)	1.68 (0.82, NC)	0.99 (0.62, 1.15)
	Hazard Ratio (95% CI)		0.595 (0.367, 0.965)
	Treatment P-value [a]		0.02432
	Interaction P-value [b]		0.02192
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.43 (0.27, 0.57)	4, 0.19 (0.09, 0.33)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.19 (0.09, 0.33)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.APS.KM.S4.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	58 (46.0)	47 (36.4)
	Median Survival Est. (95% CI)	1.51 (0.89, 5.32)	1.51 (0.66, 2.37)
	Hazard Ratio (95% CI)		0.962 (0.655, 1.414)
	Treatment P-value [a]		0.83977
	Interaction P-value [b]		0.31220
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.33 (0.21, 0.46)	5, 0.35 (0.23, 0.47)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.35 (0.23, 0.47)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.APS.KM.S4.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	21 (48.8)	14 (31.8)
	Median Survival Est. (95% CI)	1.05 (0.53, NC)	2.56 (1.02, NC)
	Hazard Ratio (95% CI)		1.584 (0.805, 3.117)
	Treatment P-value [a]		0.10671
	Interaction P-value [b]		0.31220
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.36 (0.20, 0.53)	2, 0.42 (0.22, 0.61)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.APS.KM.S4.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	85 (64.4)	81 (60.4)
	Median Survival Est. (95% CI)	0.99 (0.62, 1.41)	0.99 (0.43, 1.38)
	Hazard Ratio (95% CI)		0.890 (0.656, 1.207)
	Treatment P-value [a]		0.44123
	Interaction P-value [b]		0.31220
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.26 (0.18, 0.35)	6, 0.20 (0.11, 0.31)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.15 (0.06, 0.28)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.APS.KM.S5.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	74 (61.7)	65 (52.4)
	Median Survival Est. (95% CI)	1.08 (0.76, 1.54)	1.02 (0.62, 1.87)
	Hazard Ratio (95% CI)		0.970 (0.695, 1.354)
	Treatment P-value [a]		0.82584
	Interaction P-value [b]		0.94206
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.29 (0.20, 0.38)	5, 0.28 (0.16, 0.42)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.21 (0.08, 0.38)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.APS.KM.S5.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	90 (49.7)	77 (42.1)
	Median Survival Est. (95% CI)	1.25 (0.79, 1.71)	1.28 (0.76, 1.94)
	Hazard Ratio (95% CI)		0.986 (0.727, 1.337)
	Treatment P-value [a]		0.93101
	Interaction P-value [b]		0.94206
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.33 (0.24, 0.42)	8, 0.26 (0.17, 0.36)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.26 (0.17, 0.36)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.APS.KM.S6.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	43 (46.2)	39 (41.1)
	Median Survival Est. (95% CI)	1.28 (0.69, 9.07)	1.28 (0.66, 2.10)
	Hazard Ratio (95% CI)		0.851 (0.551, 1.313)
	Treatment P-value [a]		0.45140
	Interaction P-value [b]		0.45229
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.40 (0.28, 0.51)	2, 0.23 (0.10, 0.38)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.23 (0.10, 0.38)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.APS.KM.S6.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	121 (58.2)	103 (48.6)
	Median Survival Est. (95% CI)	1.02 (0.79, 1.51)	1.05 (0.76, 1.87)
	Hazard Ratio (95% CI)		1.034 (0.795, 1.345)
	Treatment P-value [a]		0.76685
	Interaction P-value [b]		0.45229
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.27 (0.20, 0.35)	11, 0.29 (0.21, 0.38)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.26 (0.17, 0.36)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.APS.KM.S7.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	83 (58.9)	43 (38.4)
	Median Survival Est. (95% CI)	1.02 (0.76, 1.54)	1.91 (1.18, NC)
	Hazard Ratio (95% CI)		1.381 (0.955, 1.996)
	Treatment P-value [a]		0.07220
	Interaction P-value [b]		0.06687
6 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.26 (0.16, 0.36)	5, 0.38 (0.26, 0.51)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.APS.KM.S7.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	47 (54.0)	63 (53.8)
	Median Survival Est. (95% CI)	1.02 (0.56, 1.64)	0.99 (0.36, 1.08)
	Hazard Ratio (95% CI)		0.760 (0.521, 1.110)
	Treatment P-value [a]		0.15958
	Interaction P-value [b]		0.06687
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.34 (0.23, 0.45)	4, 0.18 (0.08, 0.31)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.14 (0.05, 0.28)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.APS.KM.S7.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	34 (46.6)	36 (46.2)
	Median Survival Est. (95% CI)	1.51 (0.79, 5.32)	1.08 (0.56, 1.77)
	Hazard Ratio (95% CI)		0.850 (0.532, 1.359)
	Treatment P-value [a]		0.45080
	Interaction P-value [b]		0.06687
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.35 (0.20, 0.50)	4, 0.29 (0.16, 0.43)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.29 (0.16, 0.43)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.APS.KM.S8.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	50 (51.0)	61 (57.0)
	Median Survival Est. (95% CI)	1.22 (0.76, 1.74)	0.99 (0.53, 1.71)
	Hazard Ratio (95% CI)		0.799 (0.550, 1.162)
	Treatment P-value [a]		0.23008
	Interaction P-value [b]		0.17397
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.34 (0.23, 0.46)	6, 0.21 (0.11, 0.33)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.APS.KM.S8.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	114 (56.2)	81 (40.5)
	Median Survival Est. (95% CI)	1.05 (0.76, 1.61)	1.41 (0.99, 1.91)
	Hazard Ratio (95% CI)		1.107 (0.833, 1.473)
	Treatment P-value [a]		0.45695
	Interaction P-value [b]		0.17397
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.29 (0.21, 0.37)	7, 0.31 (0.21, 0.42)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	2, 0.31 (0.21, 0.42)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.APS.KM.S9.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	142 (54.2)	126 (46.7)
	Median Survival Est. (95% CI)	1.15 (0.82, 1.54)	1.05 (0.76, 1.64)
	Hazard Ratio (95% CI)		0.931 (0.732, 1.183)
	Treatment P-value [a]		0.56073
	Interaction P-value [b]		0.27002
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.31 (0.24, 0.38)	11, 0.26 (0.18, 0.34)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.23 (0.15, 0.32)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.APS.KM.S9.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	22 (56.4)	16 (43.2)
	Median Survival Est. (95% CI)	0.99 (0.56, 1.71)	2.37 (0.72, NC)
	Hazard Ratio (95% CI)		1.371 (0.719, 2.613)
	Treatment P-value [a]		0.32395
	Interaction P-value [b]		0.27002
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.29 (0.14, 0.46)	2, 0.40 (0.21, 0.59)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.40 (0.21, 0.59)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.APS.KM.S10.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	39 (63.9)	29 (58.0)
	Median Survival Est. (95% CI)	1.18 (0.56, 1.64)	1.02 (0.36, 2.40)
	Hazard Ratio (95% CI)		1.002 (0.620, 1.621)
	Treatment P-value [a]		0.87534
	Interaction P-value [b]		0.93989
6 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.25 (0.14, 0.38)	3, 0.25 (0.12, 0.41)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.APS.KM.S10.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	111 (53.6)	95 (44.2)
	Median Survival Est. (95% CI)	0.99 (0.79, 1.51)	1.18 (0.76, 1.77)
	Hazard Ratio (95% CI)		1.024 (0.778, 1.347)
	Treatment P-value [a]		0.86451
	Interaction P-value [b]		0.93989
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.29 (0.22, 0.37)	9, 0.28 (0.19, 0.38)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	2, 0.28 (0.19, 0.38)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

2.4.2.7 Obstipation

Astellas: 7465-CL-0301
Table EORTC15.COS.KM.S1.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	43 (39.8)	38 (34.2)
	Median Survival Est. (95% CI)	2.14 (1.12, NC)	2.69 (1.45, NC)
	Hazard Ratio (95% CI)		0.985 (0.637, 1.525)
	Treatment P-value [a]		0.87918
	Interaction P-value [b]		0.78643
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.50 (0.38, 0.60)	7, 0.44 (0.30, 0.57)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.33 (0.10, 0.59)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.COS.KM.S1.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	87 (45.1)	71 (36.2)
	Median Survival Est. (95% CI)	1.94 (1.28, 5.39)	2.56 (1.22, NC)
	Hazard Ratio (95% CI)		1.061 (0.775, 1.454)
	Treatment P-value [a]		0.73667
	Interaction P-value [b]		0.78643
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.37 (0.28, 0.46)	10, 0.43 (0.33, 0.53)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.30 (0.20, 0.42)	2, 0.43 (0.33, 0.53)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.30 (0.20, 0.42)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.COS.KM.S2.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	107 (43.0)	83 (34.7)
	Median Survival Est. (95% CI)	2.14 (1.28, 9.99)	3.78 (1.25, NC)
	Hazard Ratio (95% CI)		1.005 (0.753, 1.340)
	Treatment P-value [a]		0.94701
	Interaction P-value [b]		0.58427
6 Months	Patients at Risk, Survival Est. (95% CI)	23, 0.42 (0.34, 0.50)	14, 0.46 (0.37, 0.54)
12 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.36 (0.24, 0.49)	0
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.36 (0.24, 0.49)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.COS.KM.S2.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	23 (44.2)	26 (38.2)
	Median Survival Est. (95% CI)	2.14 (1.05, 8.08)	2.56 (1.22, NC)
	Hazard Ratio (95% CI)		1.198 (0.683, 2.101)
	Treatment P-value [a]		0.58383
	Interaction P-value [b]		0.58427
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.33 (0.13, 0.55)	3, 0.37 (0.19, 0.55)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	2, 0.37 (0.19, 0.55)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.COS.KM.S3.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	101 (42.4)	83 (35.8)
	Median Survival Est. (95% CI)	2.14 (1.25, 8.08)	2.14 (1.25, NC)
	Hazard Ratio (95% CI)		0.992 (0.741, 1.327)
	Treatment P-value [a]		0.97939
	Interaction P-value [b]		0.55388
6 Months	Patients at Risk, Survival Est. (95% CI)	22, 0.42 (0.33, 0.50)	12, 0.44 (0.35, 0.52)
12 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.36 (0.26, 0.46)	1, 0.44 (0.35, 0.52)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.36 (0.26, 0.46)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.COS.KM.S3.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	29 (46.0)	26 (34.7)
	Median Survival Est. (95% CI)	1.68 (0.99, NC)	3.91 (1.22, NC)
	Hazard Ratio (95% CI)		1.190 (0.701, 2.021)
	Treatment P-value [a]		0.54179
	Interaction P-value [b]		0.55388
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.38 (0.22, 0.54)	5, 0.43 (0.25, 0.59)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.32 (0.12, 0.54)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.COS.KM.S4.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	52 (41.3)	38 (29.5)
	Median Survival Est. (95% CI)	2.14 (1.18, 8.08)	4.34 (0.92, NC)
	Hazard Ratio (95% CI)		1.042 (0.686, 1.583)
	Treatment P-value [a]		0.82965
	Interaction P-value [b]		0.14558
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.39 (0.26, 0.51)	6, 0.48 (0.35, 0.60)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.48 (0.35, 0.60)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.COS.KM.S4.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	11 (25.6)	17 (38.6)
	Median Survival Est. (95% CI)	5.55 (1.08, NC)	1.22 (0.82, NC)
	Hazard Ratio (95% CI)		0.519 (0.243, 1.110)
	Treatment P-value [a]		0.10118
	Interaction P-value [b]		0.14558
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.48 (0.22, 0.71)	1, 0.33 (0.15, 0.53)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.48 (0.22, 0.71)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.COS.KM.S4.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	67 (50.8)	54 (40.3)
	Median Survival Est. (95% CI)	1.45 (1.18, 8.08)	3.91 (1.64, NC)
	Hazard Ratio (95% CI)		1.204 (0.840, 1.726)
	Treatment P-value [a]		0.28603
	Interaction P-value [b]		0.14558
6 Months	Patients at Risk, Survival Est. (95% CI)	15, 0.41 (0.31, 0.50)	10, 0.43 (0.32, 0.55)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.36 (0.24, 0.48)	1, 0.43 (0.32, 0.55)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.36 (0.24, 0.48)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.COS.KM.S5.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	56 (46.7)	49 (39.5)
	Median Survival Est. (95% CI)	2.60 (1.18, NC)	3.78 (1.18, NC)
	Hazard Ratio (95% CI)		1.031 (0.701, 1.517)
	Treatment P-value [a]		0.87149
	Interaction P-value [b]		0.99451
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.46 (0.36, 0.56)	9, 0.44 (0.31, 0.56)
12 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.36 (0.20, 0.51)	1, 0.44 (0.31, 0.56)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.36 (0.20, 0.51)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.COS.KM.S5.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	74 (40.9)	60 (32.8)
	Median Survival Est. (95% CI)	2.14 (1.22, 5.52)	2.14 (1.25, NC)
	Hazard Ratio (95% CI)		1.033 (0.735, 1.453)
	Treatment P-value [a]		0.84369
	Interaction P-value [b]		0.99451
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.35 (0.25, 0.46)	8, 0.43 (0.31, 0.53)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.35 (0.20, 0.51)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.COS.KM.S6.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	33 (35.5)	32 (33.7)
	Median Survival Est. (95% CI)	3.29 (1.18, NC)	1.61 (1.18, NC)
	Hazard Ratio (95% CI)		0.798 (0.491, 1.299)
	Treatment P-value [a]		0.42186
	Interaction P-value [b]		0.22301
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.48 (0.35, 0.61)	1, 0.37 (0.22, 0.52)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.37 (0.22, 0.52)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.COS.KM.S6.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	97 (46.6)	77 (36.3)
	Median Survival Est. (95% CI)	1.94 (1.22, 5.52)	4.34 (1.64, NC)
	Hazard Ratio (95% CI)		1.139 (0.844, 1.538)
	Treatment P-value [a]		0.39362
	Interaction P-value [b]		0.22301
6 Months	Patients at Risk, Survival Est. (95% CI)	16, 0.38 (0.29, 0.47)	16, 0.46 (0.36, 0.55)
12 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.32 (0.22, 0.43)	1, 0.41 (0.29, 0.53)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.32 (0.22, 0.43)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.COS.KM.S7.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	66 (46.8)	38 (33.9)
	Median Survival Est. (95% CI)	1.38 (1.08, 3.81)	3.78 (1.64, NC)
	Hazard Ratio (95% CI)		1.279 (0.858, 1.908)
	Treatment P-value [a]		0.20757
	Interaction P-value [b]		0.29422
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.35 (0.25, 0.46)	3, 0.42 (0.25, 0.57)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.35 (0.25, 0.46)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Astellas: 7465-CL-0301
Table EORTC15.COS.KM.S7.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	35 (40.2)	41 (35.0)
	Median Survival Est. (95% CI)	5.52 (1.25, NC)	3.91 (1.18, NC)
	Hazard Ratio (95% CI)		0.936 (0.594, 1.475)
	Treatment P-value [a]		0.78547
	Interaction P-value [b]		0.29422
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.43 (0.28, 0.57)	9, 0.46 (0.33, 0.58)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.37 (0.20, 0.53)	1, 0.46 (0.33, 0.58)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.37 (0.20, 0.53)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.COS.KM.S7.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	29 (39.7)	30 (38.5)
	Median Survival Est. (95% CI)	2.43 (1.18, NC)	1.48 (0.72, NC)
	Hazard Ratio (95% CI)		0.778 (0.467, 1.297)
	Treatment P-value [a]		0.35254
	Interaction P-value [b]		0.29422
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.50 (0.36, 0.63)	5, 0.40 (0.25, 0.54)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.40 (0.25, 0.54)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.COS.KM.S8.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	43 (43.9)	49 (45.8)
	Median Survival Est. (95% CI)	1.54 (1.08, NC)	1.25 (0.99, 5.36)
	Hazard Ratio (95% CI)		0.874 (0.580, 1.316)
	Treatment P-value [a]		0.52925
	Interaction P-value [b]		0.26893
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.39 (0.26, 0.51)	3, 0.33 (0.19, 0.48)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.19 (0.02, 0.50)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.COS.KM.S8.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	87 (42.9)	60 (30.0)
	Median Survival Est. (95% CI)	2.60 (1.31, 8.08)	4.67 (1.74, NC)
	Hazard Ratio (95% CI)		1.175 (0.845, 1.635)
	Treatment P-value [a]		0.32099
	Interaction P-value [b]		0.26893
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.42 (0.33, 0.51)	14, 0.49 (0.39, 0.59)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.35 (0.24, 0.47)	2, 0.44 (0.30, 0.57)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.35 (0.24, 0.47)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.COS.KM.S9.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	115 (43.9)	96 (35.6)
	Median Survival Est. (95% CI)	2.10 (1.22, 5.39)	2.56 (1.48, 8.11)
	Hazard Ratio (95% CI)		1.040 (0.793, 1.364)
	Treatment P-value [a]		0.80093
	Interaction P-value [b]		0.89216
6 Months	Patients at Risk, Survival Est. (95% CI)	23, 0.39 (0.31, 0.47)	14, 0.42 (0.33, 0.50)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.29 (0.17, 0.42)	1, 0.37 (0.26, 0.48)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.COS.KM.S9.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	15 (38.5)	13 (35.1)
	Median Survival Est. (95% CI)	19.12 (1.08, NC)	NC (0.79, NC)
	Hazard Ratio (95% CI)		0.984 (0.462, 2.094)
	Treatment P-value [a]		0.98043
	Interaction P-value [b]		0.89216
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.54 (0.34, 0.69)	3, 0.56 (0.36, 0.71)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.54 (0.34, 0.69)	1, 0.56 (0.36, 0.71)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.54 (0.34, 0.69)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.COS.KM.S10.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	35 (57.4)	17 (34.0)
	Median Survival Est. (95% CI)	1.22 (0.99, 5.39)	NC (1.48, NC)
	Hazard Ratio (95% CI)		1.673 (0.937, 2.987)
	Treatment P-value [a]		0.08317
	Interaction P-value [b]		0.08013
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.34 (0.20, 0.48)	3, 0.56 (0.38, 0.70)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.COS.KM.S10.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	85 (41.1)	78 (36.3)
	Median Survival Est. (95% CI)	2.14 (1.38, 8.08)	1.71 (1.22, NC)
	Hazard Ratio (95% CI)		0.931 (0.684, 1.267)
	Treatment P-value [a]		0.65928
	Interaction P-value [b]		0.08013
6 Months	Patients at Risk, Survival Est. (95% CI)	18, 0.42 (0.33, 0.51)	13, 0.40 (0.31, 0.50)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.30 (0.16, 0.47)	2, 0.40 (0.31, 0.50)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.30 (0.16, 0.47)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

2.4.2.8 Diarrhö

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Table EORTC15.DIS.KM.S1.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	43 (39.8)	38 (34.2)
	Median Survival Est. (95% CI)	7.56 (0.95, NC)	5.32 (1.25, NC)
	Hazard Ratio (95% CI)		1.031 (0.666, 1.595)
	Treatment P-value [a]		0.86862
	Interaction P-value [b]		0.96964
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.50 (0.39, 0.61)	10, 0.44 (0.30, 0.58)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.DIS.KM.S1.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	86 (44.6)	76 (38.8)
	Median Survival Est. (95% CI)	1.94 (1.45, 6.83)	2.23 (1.54, 7.69)
	Hazard Ratio (95% CI)		1.020 (0.749, 1.389)
	Treatment P-value [a]		0.89783
	Interaction P-value [b]		0.96964
6 Months	Patients at Risk, Survival Est. (95% CI)	18, 0.42 (0.34, 0.51)	11, 0.42 (0.32, 0.52)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.27 (0.15, 0.41)	2, 0.23 (0.08, 0.41)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.DIS.KM.S2.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	110 (44.2)	91 (38.1)
	Median Survival Est. (95% CI)	2.10 (1.22, 7.49)	1.87 (1.28, 5.36)
	Hazard Ratio (95% CI)		0.965 (0.731, 1.275)
	Treatment P-value [a]		0.77966
	Interaction P-value [b]		0.50562
6 Months	Patients at Risk, Survival Est. (95% CI)	25, 0.46 (0.38, 0.53)	16, 0.40 (0.31, 0.49)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.25 (0.12, 0.39)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.DIS.KM.S2.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	19 (36.5)	23 (33.8)
	Median Survival Est. (95% CI)	2.23 (0.76, NC)	7.69 (1.81, NC)
	Hazard Ratio (95% CI)		1.211 (0.660, 2.225)
	Treatment P-value [a]		0.52374
	Interaction P-value [b]		0.50562
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.44 (0.26, 0.60)	5, 0.53 (0.37, 0.67)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	2, 0.40 (0.16, 0.63)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.DIS.KM.S3.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	105 (44.1)	88 (37.9)
	Median Survival Est. (95% CI)	1.94 (0.99, 6.83)	2.60 (1.58, 8.08)
	Hazard Ratio (95% CI)		1.078 (0.812, 1.432)
	Treatment P-value [a]		0.60591
	Interaction P-value [b]		0.42869
6 Months	Patients at Risk, Survival Est. (95% CI)	23, 0.43 (0.36, 0.51)	16, 0.42 (0.33, 0.51)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.28 (0.16, 0.41)	1, 0.25 (0.11, 0.42)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Table EORTC15.DIS.KM.S3.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	24 (38.1)	26 (34.7)
	Median Survival Est. (95% CI)	9.63 (1.12, NC)	4.50 (0.99, NC)
	Hazard Ratio (95% CI)		0.838 (0.481, 1.461)
	Treatment P-value [a]		0.52189
	Interaction P-value [b]		0.42869
6 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.52 (0.37, 0.66)	5, 0.46 (0.30, 0.62)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.35 (0.14, 0.57)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.DIS.KM.S4.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	53 (42.1)	31 (24.0)
	Median Survival Est. (95% CI)	1.94 (0.79, 8.18)	NC (2.00, NC)
	Hazard Ratio (95% CI)		1.744 (1.119, 2.719)
	Treatment P-value [a]		0.01320
	Interaction P-value [b]		0.00306
6 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.43 (0.31, 0.54)	11, 0.59 (0.47, 0.70)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.51 (0.32, 0.67)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.DIS.KM.S4.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	13 (30.2)	22 (50.0)
	Median Survival Est. (95% CI)	2.40 (1.45, NC)	1.02 (0.62, 1.58)
	Hazard Ratio (95% CI)		0.449 (0.226, 0.893)
	Treatment P-value [a]		0.01255
	Interaction P-value [b]		0.00306
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.44 (0.22, 0.63)	1, 0.09 (0.01, 0.31)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.DIS.KM.S4.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	63 (47.7)	61 (45.5)
	Median Survival Est. (95% CI)	1.97 (1.02, 9.63)	2.60 (1.22, 8.08)
	Hazard Ratio (95% CI)		0.889 (0.624, 1.265)
	Treatment P-value [a]		0.50326
	Interaction P-value [b]		0.00306
6 Months	Patients at Risk, Survival Est. (95% CI)	18, 0.47 (0.37, 0.56)	9, 0.40 (0.28, 0.51)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.33 (0.19, 0.49)	1, 0.15 (0.01, 0.43)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.DIS.KM.S5.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	54 (45.0)	56 (45.2)
	Median Survival Est. (95% CI)	2.92 (1.45, NC)	2.17 (1.28, 8.08)
	Hazard Ratio (95% CI)		0.852 (0.586, 1.238)
	Treatment P-value [a]		0.40071
	Interaction P-value [b]		0.19094
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.49 (0.39, 0.59)	10, 0.39 (0.27, 0.50)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.32 (0.16, 0.50)	1, 0.22 (0.06, 0.43)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.DIS.KM.S5.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	75 (41.4)	58 (31.7)
	Median Survival Est. (95% CI)	1.84 (0.99, 6.83)	5.36 (1.54, NC)
	Hazard Ratio (95% CI)		1.195 (0.848, 1.684)
	Treatment P-value [a]		0.32680
	Interaction P-value [b]		0.19094
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.42 (0.33, 0.51)	11, 0.47 (0.36, 0.58)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.26 (0.12, 0.43)	1, 0.32 (0.14, 0.51)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.DIS.KM.S6.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	37 (39.8)	30 (31.6)
	Median Survival Est. (95% CI)	1.74 (0.76, NC)	2.00 (1.02, NC)
	Hazard Ratio (95% CI)		1.106 (0.683, 1.792)
	Treatment P-value [a]		0.61249
	Interaction P-value [b]		0.71039
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.41 (0.28, 0.53)	3, 0.49 (0.35, 0.61)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.25 (0.02, 0.60)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.DIS.KM.S6.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	92 (44.2)	84 (39.6)
	Median Survival Est. (95% CI)	2.17 (1.45, 8.18)	2.79 (1.61, 8.08)
	Hazard Ratio (95% CI)		0.994 (0.739, 1.336)
	Treatment P-value [a]		0.95967
	Interaction P-value [b]		0.71039
6 Months	Patients at Risk, Survival Est. (95% CI)	21, 0.47 (0.39, 0.55)	18, 0.42 (0.33, 0.51)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.28 (0.15, 0.43)	1, 0.27 (0.13, 0.43)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.DIS.KM.S7.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	66 (46.8)	35 (31.3)
	Median Survival Est. (95% CI)	1.84 (0.95, 7.49)	7.69 (1.87, NC)
	Hazard Ratio (95% CI)		1.426 (0.945, 2.150)
	Treatment P-value [a]		0.09146
	Interaction P-value [b]		0.00019
6 Months	Patients at Risk, Survival Est. (95% CI)	14, 0.41 (0.32, 0.51)	8, 0.51 (0.37, 0.64)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.28 (0.14, 0.43)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.DIS.KM.S7.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	34 (39.1)	60 (51.3)
	Median Survival Est. (95% CI)	2.23 (1.74, NC)	0.99 (0.59, 1.68)
	Hazard Ratio (95% CI)		0.509 (0.334, 0.776)
	Treatment P-value [a]		0.00201
	Interaction P-value [b]		0.00019
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.47 (0.34, 0.59)	3, 0.21 (0.10, 0.35)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.11 (0.01, 0.32)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.DIS.KM.S7.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	29 (39.7)	19 (24.4)
	Median Survival Est. (95% CI)	6.83 (0.79, 9.33)	NC (2.17, NC)
	Hazard Ratio (95% CI)		1.867 (1.046, 3.332)
	Treatment P-value [a]		0.02605
	Interaction P-value [b]		0.00019
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.52 (0.38, 0.64)	10, 0.64 (0.48, 0.76)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.53 (0.29, 0.72)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.DIS.KM.S8.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	42 (42.9)	44 (41.1)
	Median Survival Est. (95% CI)	1.77 (0.99, NC)	4.50 (1.71, 8.08)
	Hazard Ratio (95% CI)		1.108 (0.726, 1.692)
	Treatment P-value [a]		0.60888
	Interaction P-value [b]		0.62977
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.43 (0.31, 0.54)	9, 0.44 (0.31, 0.56)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.37 (0.23, 0.51)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.DIS.KM.S8.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	87 (42.9)	70 (35.0)
	Median Survival Est. (95% CI)	2.23 (1.02, 8.18)	1.81 (1.28, NC)
	Hazard Ratio (95% CI)		0.973 (0.710, 1.334)
	Treatment P-value [a]		0.86657
	Interaction P-value [b]		0.62977
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.47 (0.38, 0.55)	12, 0.43 (0.32, 0.52)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.26 (0.13, 0.41)	2, 0.35 (0.21, 0.50)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.DIS.KM.S9.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	111 (42.4)	99 (36.7)
	Median Survival Est. (95% CI)	2.14 (1.45, 7.56)	2.79 (1.54, 7.69)
	Hazard Ratio (95% CI)		0.997 (0.760, 1.308)
	Treatment P-value [a]		0.94588
	Interaction P-value [b]		0.59978
6 Months	Patients at Risk, Survival Est. (95% CI)	27, 0.46 (0.39, 0.53)	19, 0.43 (0.35, 0.52)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.30 (0.18, 0.42)	1, 0.23 (0.09, 0.41)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.DIS.KM.S9.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	18 (46.2)	15 (40.5)
	Median Survival Est. (95% CI)	2.10 (0.72, NC)	3.25 (1.02, NC)
	Hazard Ratio (95% CI)		1.215 (0.611, 2.413)
	Treatment P-value [a]		0.60859
	Interaction P-value [b]		0.59978
6 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.38 (0.20, 0.57)	2, 0.41 (0.18, 0.62)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.41 (0.18, 0.62)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.DIS.KM.S10.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	31 (50.8)	15 (30.0)
	Median Survival Est. (95% CI)	1.51 (0.82, NC)	8.77 (5.32, NC)
	Hazard Ratio (95% CI)		1.770 (0.955, 3.280)
	Treatment P-value [a]		0.07135
	Interaction P-value [b]		0.08761
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.39 (0.25, 0.53)	7, 0.56 (0.34, 0.74)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.39 (0.25, 0.53)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.DIS.KM.S10.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	86 (41.5)	81 (37.7)
	Median Survival Est. (95% CI)	2.20 (1.12, 7.56)	2.14 (1.28, 7.69)
	Hazard Ratio (95% CI)		0.972 (0.717, 1.317)
	Treatment P-value [a]		0.87528
	Interaction P-value [b]		0.08761
6 Months	Patients at Risk, Survival Est. (95% CI)	21, 0.46 (0.38, 0.54)	12, 0.42 (0.33, 0.51)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.23 (0.11, 0.39)	2, 0.33 (0.20, 0.46)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

2.4.2.9 Finanzielle Schwierigkeiten

Astellas: 7465-CL-0301
Table EORTC15.FIS.KM.S1.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	33 (30.6)	23 (20.7)
	Median Survival Est. (95% CI)	8.38 (5.36, NC)	NC (5.32, NC)
	Hazard Ratio (95% CI)		1.336 (0.784, 2.275)
	Treatment P-value [a]		0.29405
	Interaction P-value [b]		0.15628
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.62 (0.49, 0.72)	11, 0.63 (0.48, 0.75)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.43 (0.22, 0.62)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.FIS.KM.S1.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	48 (24.9)	49 (25.0)
	Median Survival Est. (95% CI)	NC (8.15, NC)	9.00 (5.42, NC)
	Hazard Ratio (95% CI)		0.826 (0.554, 1.230)
	Treatment P-value [a]		0.34220
	Interaction P-value [b]		0.15628
6 Months	Patients at Risk, Survival Est. (95% CI)	23, 0.66 (0.57, 0.74)	13, 0.59 (0.48, 0.69)
12 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.54 (0.38, 0.67)	3, 0.49 (0.29, 0.67)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.FIS.KM.S2.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	71 (28.5)	54 (22.6)
	Median Survival Est. (95% CI)	9.36 (7.56, NC)	NC (9.00, NC)
	Hazard Ratio (95% CI)		1.030 (0.723, 1.468)
	Treatment P-value [a]		0.89440
	Interaction P-value [b]		0.48095
6 Months	Patients at Risk, Survival Est. (95% CI)	32, 0.64 (0.55, 0.71)	18, 0.61 (0.50, 0.70)
12 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.46 (0.33, 0.59)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.FIS.KM.S2.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	10 (19.2)	18 (26.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (2.69, NC)
	Hazard Ratio (95% CI)		0.759 (0.350, 1.644)
	Treatment P-value [a]		0.44158
	Interaction P-value [b]		0.48095
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.71 (0.53, 0.84)	6, 0.60 (0.44, 0.73)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.71 (0.53, 0.84)	3, 0.60 (0.44, 0.73)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.FIS.KM.S3.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	66 (27.7)	56 (24.1)
	Median Survival Est. (95% CI)	NC (6.34, NC)	NC (5.42, NC)
	Hazard Ratio (95% CI)		0.991 (0.694, 1.416)
	Treatment P-value [a]		0.93576
	Interaction P-value [b]		0.86393
6 Months	Patients at Risk, Survival Est. (95% CI)	29, 0.62 (0.54, 0.70)	18, 0.60 (0.50, 0.69)
12 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.52 (0.39, 0.63)	2, 0.53 (0.37, 0.67)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.FIS.KM.S3.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	15 (23.8)	16 (21.3)
	Median Survival Est. (95% CI)	9.36 (8.15, NC)	NC (2.79, NC)
	Hazard Ratio (95% CI)		0.925 (0.457, 1.872)
	Treatment P-value [a]		0.84494
	Interaction P-value [b]		0.86393
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.72 (0.57, 0.83)	6, 0.62 (0.44, 0.76)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.62 (0.44, 0.76)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.FIS.KM.S4.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	24 (19.0)	22 (17.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI)		0.905 (0.507, 1.614)
	Treatment P-value [a]		0.71948
	Interaction P-value [b]		0.92789
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.73 (0.62, 0.81)	10, 0.68 (0.55, 0.78)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	2, 0.68 (0.55, 0.78)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.FIS.KM.S4.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	8 (18.6)	7 (15.9)
	Median Survival Est. (95% CI)	NC (5.45, NC)	NC (2.69, NC)
	Hazard Ratio (95% CI)		0.975 (0.353, 2.692)
	Treatment P-value [a]		0.99989
	Interaction P-value [b]		0.92789
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.68 (0.44, 0.83)	4, 0.70 (0.45, 0.85)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.68 (0.44, 0.83)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.FIS.KM.S4.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	49 (37.1)	43 (32.1)
	Median Survival Est. (95% CI)	8.15 (5.36, NC)	9.00 (3.98, NC)
	Hazard Ratio (95% CI)		1.041 (0.691, 1.568)
	Treatment P-value [a]		0.93680
	Interaction P-value [b]		0.92789
6 Months	Patients at Risk, Survival Est. (95% CI)	16, 0.59 (0.48, 0.68)	10, 0.54 (0.41, 0.65)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.34 (0.17, 0.52)	1, 0.36 (0.10, 0.63)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.FIS.KM.S5.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	33 (27.5)	27 (21.8)
	Median Survival Est. (95% CI)	NC (7.56, NC)	NC (NC , NC)
	Hazard Ratio (95% CI)		1.119 (0.673, 1.862)
	Treatment P-value [a]		0.63571
	Interaction P-value [b]		0.50014
6 Months	Patients at Risk, Survival Est. (95% CI)	19, 0.67 (0.55, 0.76)	11, 0.68 (0.57, 0.78)
12 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.57 (0.39, 0.71)	1, 0.68 (0.57, 0.78)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.FIS.KM.S5.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	48 (26.5)	45 (24.6)
	Median Survival Est. (95% CI)	8.38 (6.21, NC)	9.00 (2.69, NC)
	Hazard Ratio (95% CI)		0.894 (0.595, 1.344)
	Treatment P-value [a]		0.60304
	Interaction P-value [b]		0.50014
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.63 (0.53, 0.71)	13, 0.54 (0.42, 0.65)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.43 (0.25, 0.60)	2, 0.47 (0.31, 0.62)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.FIS.KM.S6.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	33 (35.5)	17 (17.9)
	Median Survival Est. (95% CI)	2.40 (1.31, NC)	NC (5.32, NC)
	Hazard Ratio (95% CI)		1.840 (1.024, 3.306)
	Treatment P-value [a]		0.03371
	Interaction P-value [b]		0.01109
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.50 (0.36, 0.62)	4, 0.64 (0.45, 0.77)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.34 (0.15, 0.54)	2, 0.64 (0.45, 0.77)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.FIS.KM.S6.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	48 (23.1)	55 (25.9)
	Median Survival Est. (95% CI)	NC (8.15, NC)	NC (5.42, NC)
	Hazard Ratio (95% CI)		0.741 (0.503, 1.091)
	Treatment P-value [a]		0.12578
	Interaction P-value [b]		0.01109
6 Months	Patients at Risk, Survival Est. (95% CI)	29, 0.70 (0.62, 0.77)	20, 0.60 (0.50, 0.68)
12 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.56 (0.41, 0.69)	1, 0.53 (0.37, 0.67)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.FIS.KM.S7.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	49 (34.8)	24 (21.4)
	Median Survival Est. (95% CI)	8.15 (2.76, NC)	NC (NC , NC)
	Hazard Ratio (95% CI)		1.348 (0.826, 2.198)
	Treatment P-value [a]		0.23876
	Interaction P-value [b]		0.16217
6 Months	Patients at Risk, Survival Est. (95% CI)	19, 0.58 (0.47, 0.67)	6, 0.65 (0.52, 0.76)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.38 (0.22, 0.53)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.FIS.KM.S7.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	20 (23.0)	30 (25.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	9.00 (5.32, NC)
	Hazard Ratio (95% CI)		0.742 (0.421, 1.308)
	Treatment P-value [a]		0.26909
	Interaction P-value [b]		0.16217
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.66 (0.51, 0.77)	10, 0.56 (0.40, 0.69)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.66 (0.51, 0.77)	1, 0.42 (0.17, 0.66)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.FIS.KM.S7.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	12 (16.4)	18 (23.1)
	Median Survival Est. (95% CI)	NC (6.21, NC)	NC (2.40, NC)
	Hazard Ratio (95% CI)		0.661 (0.318, 1.372)
	Treatment P-value [a]		0.24813
	Interaction P-value [b]		0.16217
6 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.78 (0.63, 0.87)	8, 0.62 (0.47, 0.75)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	2, 0.62 (0.47, 0.75)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.FIS.KM.S8.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	29 (29.6)	27 (25.2)
	Median Survival Est. (95% CI)	8.15 (6.21, NC)	NC (5.32, NC)
	Hazard Ratio (95% CI)		1.116 (0.660, 1.885)
	Treatment P-value [a]		0.71068
	Interaction P-value [b]		0.55199
6 Months	Patients at Risk, Survival Est. (95% CI)	15, 0.65 (0.51, 0.75)	11, 0.61 (0.47, 0.73)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.37 (0.17, 0.57)	1, 0.53 (0.32, 0.70)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.FIS.KM.S8.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	52 (25.6)	45 (22.5)
	Median Survival Est. (95% CI)	NC (8.38, NC)	NC (5.42, NC)
	Hazard Ratio (95% CI)		0.914 (0.613, 1.362)
	Treatment P-value [a]		0.70542
	Interaction P-value [b]		0.55199
6 Months	Patients at Risk, Survival Est. (95% CI)	21, 0.64 (0.55, 0.72)	13, 0.60 (0.49, 0.70)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.59 (0.45, 0.70)	2, 0.60 (0.49, 0.70)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.FIS.KM.S9.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	66 (25.2)	64 (23.7)
	Median Survival Est. (95% CI)	NC (8.15, NC)	NC (9.00, NC)
	Hazard Ratio (95% CI)		0.901 (0.638, 1.271)
	Treatment P-value [a]		0.54838
	Interaction P-value [b]		0.20580
6 Months	Patients at Risk, Survival Est. (95% CI)	32, 0.66 (0.58, 0.73)	22, 0.60 (0.50, 0.68)
12 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.52 (0.38, 0.64)	2, 0.53 (0.38, 0.66)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.FIS.KM.S9.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	15 (38.5)	8 (21.6)
	Median Survival Est. (95% CI)	6.34 (1.71, NC)	NC (2.69, NC)
	Hazard Ratio (95% CI)		1.636 (0.693, 3.861)
	Treatment P-value [a]		0.26245
	Interaction P-value [b]		0.20580
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.54 (0.34, 0.70)	2, 0.70 (0.46, 0.84)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.40 (0.15, 0.64)	1, 0.70 (0.46, 0.84)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.FIS.KM.S10.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	17 (27.9)	18 (36.0)
	Median Survival Est. (95% CI)	NC (8.15, NC)	2.66 (1.08, NC)
	Hazard Ratio (95% CI)		0.567 (0.292, 1.101)
	Treatment P-value [a]		0.07653
	Interaction P-value [b]		0.05656
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.67 (0.51, 0.79)	3, 0.48 (0.30, 0.65)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.50 (0.19, 0.75)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.FIS.KM.S10.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	59 (28.5)	47 (21.9)
	Median Survival Est. (95% CI)	8.38 (6.21, NC)	NC (9.00, NC)
	Hazard Ratio (95% CI)		1.195 (0.814, 1.754)
	Treatment P-value [a]		0.36109
	Interaction P-value [b]		0.05656
6 Months	Patients at Risk, Survival Est. (95% CI)	24, 0.61 (0.52, 0.69)	18, 0.63 (0.53, 0.72)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.49 (0.35, 0.61)	3, 0.56 (0.39, 0.70)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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2.4.3 MMRM-Modell

2.4.3.1 Fatigue

Astellas: 7465-CL-0301
Table EORTC.FS.MM.S1.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Fatigue Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Age Group 1

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
<65 years	N, n	108, 85	111, 68	
	Baseline Mean (SD)	36.21 (23.08)	32.19 (23.05)	
	Change from Baseline LS Mean (SE)	2.21 (1.70)	4.37 (1.89)	-2.17 (-7.16, 2.83)
	Treatment P-value			0.39448
	Hedge's g (95% CI)			-0.12 (-0.43, 0.20)
>=65 years	N, n	193, 147	196, 128	
	Baseline Mean (SD)	31.29 (24.43)	32.81 (23.98)	
	Change from Baseline LS Mean (SE)	7.46 (1.30)	12.35 (1.41)	-4.90 (-8.66, -1.13)
	Treatment P-value			0.01098
	Hedge's g (95% CI)			-0.24 (-0.47, 0.00)
	Interaction P-value [b]			0.17891

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.FS.MM.S2.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Fatigue Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Age Group 2

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
<75 years	N, n	249, 195	239, 150	
	Baseline Mean (SD)	33.39 (23.70)	32.52 (23.77)	
	Change from Baseline LS Mean (SE)	4.39 (1.13)	8.19 (1.30)	-3.80 (-7.18, -0.42)
	Treatment P-value			0.02751
	Hedge's g (95% CI)			-0.19 (-0.40, 0.02)
>=75 years	N, n	52, 37	68, 46	
	Baseline Mean (SD)	31.53 (25.86)	32.85 (23.30)	
	Change from Baseline LS Mean (SE)	11.92 (2.64)	13.95 (2.37)	-2.02 (-8.99, 4.95)
	Treatment P-value			0.56883
	Hedge's g (95% CI)			-0.10 (-0.53, 0.33)
	Interaction P-value [b]			0.82991

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.FS.MM.S3.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Fatigue Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Gender

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Male	N, n	238, 182	232, 150	
	Baseline Mean (SD)	32.84 (24.36)	31.33 (23.07)	
	Change from Baseline LS Mean (SE)	6.03 (1.18)	10.38 (1.31)	-4.34 (-7.81, -0.88)
	Treatment P-value			0.01413
	Hedge's g (95% CI)			-0.21 (-0.43, 0.01)
Female	N, n	63, 50	75, 46	
	Baseline Mean (SD)	34.00 (22.94)	36.71 (25.11)	
	Change from Baseline LS Mean (SE)	3.63 (2.26)	6.56 (2.37)	-2.94 (-9.37, 3.49)
	Treatment P-value			0.36983
	Hedge's g (95% CI)			-0.16 (-0.56, 0.24)
	Interaction P-value [b]			0.67023

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.FS.MM.S4.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Fatigue Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Region

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Western Europe	N, n	126, 90	129, 70	
	Baseline Mean (SD)	34.94 (25.29)	37.46 (27.10)	
	Change from Baseline LS Mean (SE)	4.19 (1.65)	14.59 (1.91)	-10.40 (-15.36, -5.44)
	Treatment P-value			0.00005
	Hedge's g (95% CI)			-0.48 (-0.80, -0.17)
US	N, n	43, 28	44, 24	
	Baseline Mean (SD)	31.35 (23.82)	30.09 (23.28)	
	Change from Baseline LS Mean (SE)	5.53 (3.03)	11.04 (3.23)	-5.52 (-14.22, 3.19)
	Treatment P-value			0.21346
	Hedge's g (95% CI)			-0.30 (-0.84, 0.24)

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.FS.MM.S4.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Fatigue Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Region

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Rest of the World	N, n	132, 114	134, 102	
	Baseline Mean (SD)	32.07 (23.13)	29.85 (20.62)	
	Change from Baseline LS Mean (SE)	6.52 (1.45)	5.81 (1.54)	0.71 (-3.45, 4.87)
	Treatment P-value			0.73686
	Hedge's g (95% CI)			0.04 (-0.23, 0.30)
	Interaction P-value [b]			0.00789

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.FS.MM.S5.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Fatigue Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
0	N, n	120, 102	124, 92	
	Baseline Mean (SD)	23.86 (19.55)	26.57 (21.47)	
	Change from Baseline LS Mean (SE)	8.43 (1.52)	7.33 (1.62)	1.10 (-3.27, 5.47)
	Treatment P-value			0.62042
	Hedge's g (95% CI)			0.06 (-0.22, 0.34)
1	N, n	181, 130	183, 104	
	Baseline Mean (SD)	40.34 (24.75)	37.93 (24.22)	
	Change from Baseline LS Mean (SE)	2.92 (1.39)	11.40 (1.56)	-8.48 (-12.58, -4.38)
	Treatment P-value			0.00006
	Hedge's g (95% CI)			-0.40 (-0.66, -0.14)
	Interaction P-value [b]			0.02920

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC.FS.MM.S6.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Fatigue Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Yes	N, n	93, 63	95, 52	
	Baseline Mean (SD)	38.62 (24.02)	33.97 (21.83)	
	Change from Baseline LS Mean (SE)	1.98 (2.01)	13.09 (2.25)	-11.11 (-17.05, -5.17)
	Treatment P-value			0.00027
	Hedge's g (95% CI)			-0.50 (-0.87, -0.13)
No	N, n	208, 169	212, 144	
	Baseline Mean (SD)	31.03 (23.75)	32.10 (24.27)	
	Change from Baseline LS Mean (SE)	6.75 (1.22)	8.27 (1.33)	-1.52 (-5.08, 2.03)
	Treatment P-value			0.39971
	Hedge's g (95% CI)			-0.08 (-0.30, 0.14)
	Interaction P-value [b]			0.25588

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
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Astellas: 7465-CL-0301
Table EORTC.FS.MM.S7.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Fatigue Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Paclitaxel	N, n	141, 115	112, 72	
	Baseline Mean (SD)	35.27 (23.14)	29.01 (21.55)	
	Change from Baseline LS Mean (SE)	4.33 (1.45)	7.67 (1.83)	-3.33 (-7.93, 1.27)
	Treatment P-value			0.15514
	Hedge's g (95% CI)			-0.17 (-0.47, 0.12)
Docetaxel	N, n	87, 65	117, 77	
	Baseline Mean (SD)	29.06 (21.58)	31.46 (20.34)	
	Change from Baseline LS Mean (SE)	7.49 (1.94)	8.01 (1.82)	-0.52 (-5.74, 4.70)
	Treatment P-value			0.84470
	Hedge's g (95% CI)			-0.03 (-0.36, 0.30)

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.FS.MM.S7.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Fatigue Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Vinflunine	N, n	73, 52	78, 47	
	Baseline Mean (SD)	33.33 (28.26)	39.95 (29.73)	
	Change from Baseline LS Mean (SE)	5.44 (2.22)	14.88 (2.33)	-9.43 (-15.76, -3.10)
	Treatment P-value			0.00359
	Hedge's g (95% CI)			-0.40 (-0.80, -0.01)
	Interaction P-value [b]			0.08127

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.FS.MM.S8.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Fatigue Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Primary Site of Tumor

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Upper Tract	N, n	98, 75	107, 76	
	Baseline Mean (SD)	35.85 (25.81)	33.19 (24.84)	
	Change from Baseline LS Mean (SE)	3.33 (1.83)	8.63 (1.83)	-5.30 (-10.38, -0.22)
	Treatment P-value			0.04090
	Hedge's g (95% CI)			-0.26 (-0.58, 0.06)
Other	N, n	203, 157	200, 120	
	Baseline Mean (SD)	31.78 (23.08)	32.22 (22.88)	
	Change from Baseline LS Mean (SE)	6.62 (1.28)	10.08 (1.47)	-3.46 (-7.30, 0.37)
	Treatment P-value			0.07687
	Hedge's g (95% CI)			-0.17 (-0.41, 0.07)
	Interaction P-value [b]			0.95708

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.FS.MM.S9.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Fatigue Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
1-2 lines	N, n	262, 203	270, 169	
	Baseline Mean (SD)	34.26 (24.52)	31.95 (23.64)	
	Change from Baseline LS Mean (SE)	5.05 (1.13)	10.31 (1.24)	-5.27 (-8.55, -1.98)
	Treatment P-value			0.00176
	Hedge's g (95% CI)			-0.26 (-0.46, -0.06)
>=3 lines	N, n	39, 29	37, 27	
	Baseline Mean (SD)	24.90 (18.46)	36.63 (23.43)	
	Change from Baseline LS Mean (SE)	8.32 (2.85)	4.39 (3.10)	3.93 (-4.35, 12.21)
	Treatment P-value			0.35110
	Hedge's g (95% CI)			0.20 (-0.32, 0.72)
	Interaction P-value [b]			0.42887

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.FS.MM.S10.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Fatigue Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Best Response to Prior CPI

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Responder	N, n	61, 49	50, 34	
	Baseline Mean (SD)	29.02 (20.76)	30.72 (22.23)	
	Change from Baseline LS Mean (SE)	9.07 (2.27)	10.08 (2.77)	-1.02 (-8.06, 6.03)
	Treatment P-value			0.77689
	Hedge's g (95% CI)			-0.05 (-0.48, 0.38)
Non-responder	N, n	207, 156	215, 136	
	Baseline Mean (SD)	34.47 (25.06)	34.31 (24.44)	
	Change from Baseline LS Mean (SE)	4.41 (1.30)	9.07 (1.41)	-4.66 (-8.42, -0.90)
	Treatment P-value			0.01540
	Hedge's g (95% CI)			-0.23 (-0.46, 0.00)
	Interaction P-value [b]			0.97632

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

2.4.3.2 Übelkeit und Erbrechen

Astellas: 7465-CL-0301
Table EORTC.NVS.MM.S1.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Nausea and Vomiting Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Age Group 1

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
<65 years	N, n	108, 85	111, 68	
	Baseline Mean (SD)	7.06 (14.63)	8.33 (15.64)	
	Change from Baseline LS Mean (SE)	1.72 (0.96)	2.37 (1.07)	-0.66 (-3.49, 2.18)
	Treatment P-value			0.64927
	Hedge's g (95% CI)			-0.05 (-0.37, 0.27)
>=65 years	N, n	193, 147	196, 128	
	Baseline Mean (SD)	4.88 (12.37)	4.95 (10.53)	
	Change from Baseline LS Mean (SE)	2.88 (0.75)	2.73 (0.82)	0.14 (-2.03, 2.32)
	Treatment P-value			0.89605
	Hedge's g (95% CI)			0.01 (-0.22, 0.25)
	Interaction P-value [b]			0.33135

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
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Astellas: 7465-CL-0301
Table EORTC.NVS.MM.S2.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Nausea and Vomiting Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Age Group 2

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
<75 years	N, n	249, 195	239, 150	
	Baseline Mean (SD)	5.90 (13.57)	6.67 (13.38)	
	Change from Baseline LS Mean (SE)	2.05 (0.65)	2.62 (0.75)	-0.57 (-2.52, 1.37)
	Treatment P-value			0.56300
	Hedge's g (95% CI)			-0.04 (-0.26, 0.17)
>=75 years	N, n	52, 37	68, 46	
	Baseline Mean (SD)	4.50 (11.55)	4.35 (9.58)	
	Change from Baseline LS Mean (SE)	4.80 (1.50)	2.43 (1.34)	2.37 (-1.57, 6.31)
	Treatment P-value			0.23809
	Hedge's g (95% CI)			0.21 (-0.22, 0.64)
	Interaction P-value [b]			0.18001

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.NVS.MM.S3.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Nausea and Vomiting Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Gender

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Male	N, n	238, 182	232, 150	
	Baseline Mean (SD)	4.58 (12.15)	5.44 (12.14)	
	Change from Baseline LS Mean (SE)	2.43 (0.68)	2.45 (0.75)	-0.02 (-2.01, 1.96)
	Treatment P-value			0.98295
	Hedge's g (95% CI)			-0.00 (-0.22, 0.21)
Female	N, n	63, 50	75, 46	
	Baseline Mean (SD)	9.67 (16.18)	8.33 (13.94)	
	Change from Baseline LS Mean (SE)	2.48 (1.26)	2.91 (1.33)	-0.43 (-4.03, 3.17)
	Treatment P-value			0.81499
	Hedge's g (95% CI)			-0.03 (-0.43, 0.36)
	Interaction P-value [b]			0.61258

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.NVS.MM.S4.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Nausea and Vomiting Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Region

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Western Europe	N, n	126, 90	129, 70	
	Baseline Mean (SD)	3.89 (10.61)	5.95 (12.05)	
	Change from Baseline LS Mean (SE)	3.52 (0.94)	4.26 (1.09)	-0.74 (-3.57, 2.09)
	Treatment P-value			0.60789
	Hedge's g (95% CI)			-0.05 (-0.36, 0.26)
US	N, n	43, 28	44, 24	
	Baseline Mean (SD)	8.93 (17.26)	2.78 (8.03)	
	Change from Baseline LS Mean (SE)	0.52 (1.70)	7.16 (1.82)	-6.64 (-11.54, -1.74)
	Treatment P-value			0.00799
	Hedge's g (95% CI)			-0.49 (-1.03, 0.06)

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.NVS.MM.S4.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Nausea and Vomiting Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Region

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Rest of the World	N, n	132, 114	134, 102	
	Baseline Mean (SD)	6.29 (13.92)	7.03 (13.76)	
	Change from Baseline LS Mean (SE)	1.97 (0.82)	0.45 (0.89)	1.52 (-0.86, 3.90)
	Treatment P-value			0.20983
	Hedge's g (95% CI)			0.13 (-0.13, 0.40)
	Interaction P-value [b]			0.40415

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC.NVS.MM.S5.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Nausea and Vomiting Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
0	N, n	120, 102	124, 92	
	Baseline Mean (SD)	5.23 (13.05)	5.98 (12.25)	
	Change from Baseline LS Mean (SE)	1.82 (0.87)	0.97 (0.93)	0.85 (-1.64, 3.34)
	Treatment P-value			0.50227
	Hedge's g (95% CI)			0.07 (-0.21, 0.35)
1	N, n	181, 130	183, 104	
	Baseline Mean (SD)	6.03 (13.45)	6.25 (12.97)	
	Change from Baseline LS Mean (SE)	2.93 (0.80)	4.10 (0.90)	-1.17 (-3.54, 1.20)
	Treatment P-value			0.33181
	Hedge's g (95% CI)			-0.09 (-0.34, 0.17)
	Interaction P-value [b]			0.69305

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.NVS.MM.S6.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Nausea and Vomiting Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Yes	N, n	93, 63	95, 52	
	Baseline Mean (SD)	8.73 (16.36)	5.45 (12.23)	
	Change from Baseline LS Mean (SE)	0.82 (1.13)	4.43 (1.28)	-3.61 (-6.96, -0.25)
	Treatment P-value			0.03541
	Hedge's g (95% CI)			-0.26 (-0.62, 0.11)
No	N, n	208, 169	212, 144	
	Baseline Mean (SD)	4.54 (11.75)	6.37 (12.77)	
	Change from Baseline LS Mean (SE)	2.98 (0.70)	1.95 (0.76)	1.03 (-1.00, 3.06)
	Treatment P-value			0.31810
	Hedge's g (95% CI)			0.08 (-0.14, 0.31)
	Interaction P-value [b]			0.94591

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.NVS.MM.S7.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Nausea and Vomiting Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Paclitaxel	N, n	141, 115	112, 72	
	Baseline Mean (SD)	6.09 (13.12)	5.32 (11.47)	
	Change from Baseline LS Mean (SE)	1.76 (0.83)	1.93 (1.04)	-0.18 (-2.79, 2.44)
	Treatment P-value			0.89505
	Hedge's g (95% CI)			-0.01 (-0.31, 0.28)
Docetaxel	N, n	87, 65	117, 77	
	Baseline Mean (SD)	6.41 (14.64)	7.14 (14.42)	
	Change from Baseline LS Mean (SE)	1.81 (1.09)	2.54 (1.04)	-0.72 (-3.68, 2.24)
	Treatment P-value			0.63061
	Hedge's g (95% CI)			-0.06 (-0.39, 0.27)

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.NVS.MM.S7.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Nausea and Vomiting Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Vinflunine	N, n	73, 52	78, 47	
	Baseline Mean (SD)	3.85 (11.72)	5.67 (11.14)	
	Change from Baseline LS Mean (SE)	5.00 (1.27)	3.63 (1.31)	1.36 (-2.21, 4.94)
	Treatment P-value			0.45447
	Hedge's g (95% CI)			0.09 (-0.30, 0.48)
	Interaction P-value [b]			0.67823

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.NVS.MM.S8.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Nausea and Vomiting Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Primary Site of Tumor

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Upper Tract	N, n	98, 75	107, 76	
	Baseline Mean (SD)	8.00 (16.52)	7.02 (13.68)	
	Change from Baseline LS Mean (SE)	0.68 (1.00)	-0.05 (1.02)	0.73 (-2.08, 3.55)
	Treatment P-value			0.60928
	Hedge's g (95% CI)			0.06 (-0.26, 0.38)
Other	N, n	203, 157	200, 120	
	Baseline Mean (SD)	4.56 (11.26)	5.56 (11.90)	
	Change from Baseline LS Mean (SE)	3.32 (0.72)	4.29 (0.83)	-0.96 (-3.13, 1.21)
	Treatment P-value			0.38343
	Hedge's g (95% CI)			-0.07 (-0.31, 0.16)
	Interaction P-value [b]			0.12778

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.NVS.MM.S9.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Nausea and Vomiting Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
1-2 lines	N, n	262, 203	270, 169	
	Baseline Mean (SD)	5.83 (13.48)	6.02 (12.92)	
	Change from Baseline LS Mean (SE)	2.24 (0.65)	2.74 (0.71)	-0.50 (-2.39, 1.39)
	Treatment P-value			0.60297
	Hedge's g (95% CI)			-0.04 (-0.24, 0.16)
>=3 lines	N, n	39, 29	37, 27	
	Baseline Mean (SD)	4.60 (11.70)	6.79 (10.60)	
	Change from Baseline LS Mean (SE)	3.68 (1.55)	1.45 (1.72)	2.23 (-2.32, 6.78)
	Treatment P-value			0.33584
	Hedge's g (95% CI)			0.16 (-0.36, 0.68)
	Interaction P-value [b]			0.66692

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.NVS.MM.S10.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Nausea and Vomiting Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Best Response to Prior CPI

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Responder	N, n	61, 49	50, 34	
	Baseline Mean (SD)	3.06 (7.35)	6.86 (12.39)	
	Change from Baseline LS Mean (SE)	5.33 (1.26)	0.63 (1.54)	4.70 (0.78, 8.62)
	Treatment P-value			0.01897
	Hedge's g (95% CI)			0.34 (-0.10, 0.78)
Non-responder	N, n	207, 156	215, 136	
	Baseline Mean (SD)	5.88 (13.63)	6.37 (12.84)	
	Change from Baseline LS Mean (SE)	2.51 (0.74)	2.52 (0.81)	-0.00 (-2.17, 2.16)
	Treatment P-value			0.99712
	Hedge's g (95% CI)			-0.00 (-0.23, 0.23)
	Interaction P-value [b]			0.54326

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

2.4.3.3 Schmerz

Astellas: 7465-CL-0301
Table EORTC.PS.MM.S1.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Pain Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Age Group 1

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
<65 years	N, n	108, 85	111, 68	
	Baseline Mean (SD)	33.73 (26.10)	29.66 (25.08)	
	Change from Baseline LS Mean (SE)	-4.36 (1.74)	0.38 (1.93)	-4.74 (-9.84, 0.36)
	Treatment P-value			0.06829
	Hedge's g (95% CI)			-0.23 (-0.55, 0.09)
>=65 years	N, n	193, 147	196, 128	
	Baseline Mean (SD)	28.34 (27.41)	28.78 (25.76)	
	Change from Baseline LS Mean (SE)	-1.73 (1.33)	6.49 (1.45)	-8.22 (-12.09, -4.34)
	Treatment P-value			0.00004
	Hedge's g (95% CI)			-0.38 (-0.62, -0.14)
	Interaction P-value [b]			0.17694

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.PS.MM.S2.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Pain Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Age Group 2

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
<75 years	N, n	249, 195	239, 150	
	Baseline Mean (SD)	30.09 (26.83)	30.44 (26.25)	
	Change from Baseline LS Mean (SE)	-3.03 (1.17)	3.08 (1.34)	-6.11 (-9.60, -2.63)
	Treatment P-value			0.00062
	Hedge's g (95% CI)			-0.28 (-0.50, -0.07)
>=75 years	N, n	52, 37	68, 46	
	Baseline Mean (SD)	31.53 (28.27)	24.64 (22.43)	
	Change from Baseline LS Mean (SE)	-0.95 (2.71)	8.44 (2.42)	-9.39 (-16.53, -2.25)
	Treatment P-value			0.01007
	Hedge's g (95% CI)			-0.44 (-0.87, -0.01)
	Interaction P-value [b]			0.95545

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.PS.MM.S3.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Pain Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Gender

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Male	N, n	238, 182	232, 150	
	Baseline Mean (SD)	29.76 (27.33)	29.78 (25.88)	
	Change from Baseline LS Mean (SE)	-2.57 (1.21)	3.44 (1.34)	-6.01 (-9.56, -2.46)
	Treatment P-value			0.00095
	Hedge's g (95% CI)			-0.28 (-0.49, -0.06)
Female	N, n	63, 50	75, 46	
	Baseline Mean (SD)	32.33 (25.95)	26.81 (24.21)	
	Change from Baseline LS Mean (SE)	-3.23 (2.29)	7.15 (2.41)	-10.38 (-16.90, -3.85)
	Treatment P-value			0.00189
	Hedge's g (95% CI)			-0.51 (-0.91, -0.10)
	Interaction P-value [b]			0.50289

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.PS.MM.S4.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Pain Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Region

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Western Europe	N, n	126, 90	129, 70	
	Baseline Mean (SD)	35.19 (29.08)	31.67 (28.54)	
	Change from Baseline LS Mean (SE)	-5.17 (1.71)	7.11 (1.97)	-12.28 (-17.41, -7.16)
	Treatment P-value			<.00001
	Hedge's g (95% CI)			-0.54 (-0.86, -0.22)
US	N, n	43, 28	44, 24	
	Baseline Mean (SD)	22.02 (26.08)	27.08 (23.98)	
	Change from Baseline LS Mean (SE)	-6.42 (3.11)	0.23 (3.34)	-6.66 (-15.62, 2.31)
	Treatment P-value			0.14550
	Hedge's g (95% CI)			-0.33 (-0.87, 0.21)

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.PS.MM.S4.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Pain Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Region

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Rest of the World	N, n	132, 114	134, 102	
	Baseline Mean (SD)	28.51 (24.96)	27.78 (23.61)	
	Change from Baseline LS Mean (SE)	-0.03 (1.49)	3.40 (1.59)	-3.42 (-7.71, 0.87)
	Treatment P-value			0.11746
	Hedge's g (95% CI)			-0.17 (-0.43, 0.10)
	Interaction P-value [b]			0.22915

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.PS.MM.S5.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Pain Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
0	N, n	120, 102	124, 92	
	Baseline Mean (SD)	20.26 (22.08)	25.72 (24.01)	
	Change from Baseline LS Mean (SE)	2.58 (1.56)	2.72 (1.66)	-0.14 (-4.62, 4.34)
	Treatment P-value			0.95107
	Hedge's g (95% CI)			-0.01 (-0.29, 0.27)
1	N, n	181, 130	183, 104	
	Baseline Mean (SD)	38.21 (27.95)	32.05 (26.45)	
	Change from Baseline LS Mean (SE)	-7.39 (1.43)	5.61 (1.61)	-13.01 (-17.24, -8.78)
	Treatment P-value			<.00001
	Hedge's g (95% CI)			-0.57 (-0.83, -0.31)
	Interaction P-value [b]			0.02060

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Table EORTC.PS.MM.S6.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Pain Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Yes	N, n	93, 63	95, 52	
	Baseline Mean (SD)	36.51 (26.75)	26.60 (24.97)	
	Change from Baseline LS Mean (SE)	-8.17 (2.05)	7.97 (2.30)	-16.14 (-22.20, -10.09)
	Treatment P-value			<.00001
	Hedge's g (95% CI)			-0.67 (-1.05, -0.30)
No	N, n	208, 169	212, 144	
	Baseline Mean (SD)	28.01 (26.81)	29.98 (25.67)	
	Change from Baseline LS Mean (SE)	-0.80 (1.25)	3.07 (1.36)	-3.87 (-7.51, -0.24)
	Treatment P-value			0.03686
	Hedge's g (95% CI)			-0.19 (-0.41, 0.03)
	Interaction P-value [b]			0.36034

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.PS.MM.S7.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Pain Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Paclitaxel	N, n	141, 115	112, 72	
	Baseline Mean (SD)	30.72 (26.54)	24.77 (25.02)	
	Change from Baseline LS Mean (SE)	-2.67 (1.50)	6.42 (1.89)	-9.08 (-13.82, -4.34)
	Treatment P-value			0.00019
	Hedge's g (95% CI)			-0.41 (-0.71, -0.12)
Docetaxel	N, n	87, 65	117, 77	
	Baseline Mean (SD)	22.05 (23.77)	30.95 (22.74)	
	Change from Baseline LS Mean (SE)	0.08 (1.98)	0.63 (1.88)	-0.56 (-5.93, 4.81)
	Treatment P-value			0.83769
	Hedge's g (95% CI)			-0.03 (-0.36, 0.30)

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.PS.MM.S7.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Pain Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Vinflunine	N, n	73, 52	78, 47	
	Baseline Mean (SD)	39.74 (28.99)	32.62 (29.68)	
	Change from Baseline LS Mean (SE)	-7.25 (2.29)	6.85 (2.39)	-14.10 (-20.60, -7.59)
	Treatment P-value			0.00003
	Hedge's g (95% CI)			-0.63 (-1.03, -0.23)
	Interaction P-value [b]			0.64154

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC.PS.MM.S8.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Pain Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Primary Site of Tumor

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Upper Tract	N, n	98, 75	107, 76	
	Baseline Mean (SD)	33.56 (26.49)	25.88 (24.25)	
	Change from Baseline LS Mean (SE)	-4.66 (1.85)	5.49 (1.86)	-10.16 (-15.31, -5.00)
	Treatment P-value			0.00012
	Hedge's g (95% CI)			-0.48 (-0.81, -0.16)
Other	N, n	203, 157	200, 120	
	Baseline Mean (SD)	28.77 (27.19)	31.11 (26.10)	
	Change from Baseline LS Mean (SE)	-1.70 (1.31)	3.45 (1.50)	-5.16 (-9.07, -1.25)
	Treatment P-value			0.00988
	Hedge's g (95% CI)			-0.24 (-0.48, -0.00)
	Interaction P-value [b]			0.62463

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.PS.MM.S9.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Pain Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
1-2 lines	N, n	262, 203	270, 169	
	Baseline Mean (SD)	30.79 (27.41)	27.91 (24.77)	
	Change from Baseline LS Mean (SE)	-2.97 (1.16)	5.39 (1.27)	-8.36 (-11.73, -4.99)
	Treatment P-value			<.00001
	Hedge's g (95% CI)			-0.39 (-0.59, -0.18)
>=3 lines	N, n	39, 29	37, 27	
	Baseline Mean (SD)	27.01 (24.16)	36.42 (28.88)	
	Change from Baseline LS Mean (SE)	-1.18 (2.86)	-2.69 (3.15)	1.51 (-6.84, 9.86)
	Treatment P-value			0.72238
	Hedge's g (95% CI)			0.07 (-0.44, 0.59)
	Interaction P-value [b]			0.50378

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.PS.MM.S10.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Pain Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Best Response to Prior CPI

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Responder	N, n	61, 49	50, 34	
	Baseline Mean (SD)	24.15 (27.23)	28.43 (25.80)	
	Change from Baseline LS Mean (SE)	2.08 (2.29)	2.65 (2.80)	-0.57 (-7.68, 6.54)
	Treatment P-value			0.87452
	Hedge's g (95% CI)			-0.03 (-0.46, 0.41)
Non-responder	N, n	207, 156	215, 136	
	Baseline Mean (SD)	33.23 (27.14)	30.15 (25.78)	
	Change from Baseline LS Mean (SE)	-4.26 (1.33)	4.07 (1.44)	-8.33 (-12.18, -4.48)
	Treatment P-value			0.00003
	Hedge's g (95% CI)			-0.39 (-0.62, -0.15)
	Interaction P-value [b]			0.75996

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

2.4.3.4 Atemnot

Astellas: 7465-CL-0301
Table EORTC.DS.MM.S1.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Dyspnoea Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Age Group 1

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
<65 years	N, n	108, 85	111, 68	
	Baseline Mean (SD)	15.69 (21.57)	14.71 (21.07)	
	Change from Baseline LS Mean (SE)	2.77 (1.71)	3.35 (1.91)	-0.58 (-5.63, 4.47)
	Treatment P-value			0.82087
	Hedge's g (95% CI)			-0.03 (-0.35, 0.29)
>=65 years	N, n	193, 147	196, 128	
	Baseline Mean (SD)	17.46 (21.49)	16.93 (23.66)	
	Change from Baseline LS Mean (SE)	3.91 (1.31)	7.63 (1.43)	-3.73 (-7.54, 0.09)
	Treatment P-value			0.05555
	Hedge's g (95% CI)			-0.17 (-0.41, 0.06)
	Interaction P-value [b]			0.20422

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.DS.MM.S2.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Dyspnoea Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Age Group 2

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
<75 years	N, n	249, 195	239, 150	
	Baseline Mean (SD)	16.92 (21.50)	16.67 (24.04)	
	Change from Baseline LS Mean (SE)	2.94 (1.14)	4.99 (1.31)	-2.05 (-5.47, 1.37)
	Treatment P-value			0.23972
	Hedge's g (95% CI)			-0.10 (-0.32, 0.11)
>=75 years	N, n	52, 37	68, 46	
	Baseline Mean (SD)	16.22 (21.69)	14.49 (18.12)	
	Change from Baseline LS Mean (SE)	6.61 (2.65)	10.04 (2.39)	-3.42 (-10.44, 3.59)
	Treatment P-value			0.33762
	Hedge's g (95% CI)			-0.15 (-0.58, 0.28)
	Interaction P-value [b]			0.84458

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.DS.MM.S3.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Dyspnoea Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Gender

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Male	N, n	238, 182	232, 150	
	Baseline Mean (SD)	16.67 (21.24)	16.22 (23.09)	
	Change from Baseline LS Mean (SE)	2.72 (1.19)	6.41 (1.32)	-3.68 (-7.18, -0.19)
	Treatment P-value			0.03900
	Hedge's g (95% CI)			-0.18 (-0.40, 0.04)
Female	N, n	63, 50	75, 46	
	Baseline Mean (SD)	17.33 (22.58)	15.94 (21.93)	
	Change from Baseline LS Mean (SE)	6.33 (2.26)	5.25 (2.39)	1.07 (-5.41, 7.55)
	Treatment P-value			0.74520
	Hedge's g (95% CI)			0.05 (-0.34, 0.45)
	Interaction P-value [b]			0.28687

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.DS.MM.S4.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Dyspnoea Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Region

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Western Europe	N, n	126, 90	129, 70	
	Baseline Mean (SD)	15.93 (21.33)	19.05 (26.96)	
	Change from Baseline LS Mean (SE)	4.75 (1.68)	8.25 (1.95)	-3.50 (-8.55, 1.55)
	Treatment P-value			0.17415
	Hedge's g (95% CI)			-0.15 (-0.46, 0.16)
US	N, n	43, 28	44, 24	
	Baseline Mean (SD)	14.29 (19.09)	12.50 (19.19)	
	Change from Baseline LS Mean (SE)	3.53 (3.04)	5.45 (3.27)	-1.92 (-10.70, 6.86)
	Treatment P-value			0.66706
	Hedge's g (95% CI)			-0.09 (-0.63, 0.45)

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.DS.MM.S4.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Dyspnoea Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Region

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Rest of the World	N, n	132, 114	134, 102	
	Baseline Mean (SD)	18.13 (22.24)	15.03 (20.24)	
	Change from Baseline LS Mean (SE)	2.58 (1.48)	4.88 (1.58)	-2.30 (-6.56, 1.96)
	Treatment P-value			0.28835
	Hedge's g (95% CI)			-0.13 (-0.39, 0.14)
	Interaction P-value [b]			0.59990

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.DS.MM.S5.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Dyspnoea Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
0	N, n	120, 102	124, 92	
	Baseline Mean (SD)	13.07 (19.43)	11.59 (19.41)	
	Change from Baseline LS Mean (SE)	3.96 (1.55)	5.06 (1.65)	-1.11 (-5.56, 3.35)
	Treatment P-value			0.62563
	Hedge's g (95% CI)			-0.06 (-0.34, 0.22)
1	N, n	181, 130	183, 104	
	Baseline Mean (SD)	19.74 (22.62)	20.19 (24.76)	
	Change from Baseline LS Mean (SE)	3.05 (1.41)	7.01 (1.59)	-3.96 (-8.14, 0.22)
	Treatment P-value			0.06328
	Hedge's g (95% CI)			-0.17 (-0.43, 0.08)
	Interaction P-value [b]			0.34404

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.DS.MM.S6.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Dyspnoea Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Yes	N, n	93, 63	95, 52	
	Baseline Mean (SD)	15.87 (20.62)	17.31 (25.98)	
	Change from Baseline LS Mean (SE)	5.48 (2.01)	8.02 (2.28)	-2.54 (-8.50, 3.43)
	Treatment P-value			0.40401
	Hedge's g (95% CI)			-0.12 (-0.49, 0.24)
No	N, n	208, 169	212, 144	
	Baseline Mean (SD)	17.16 (21.85)	15.74 (21.57)	
	Change from Baseline LS Mean (SE)	2.76 (1.23)	5.52 (1.34)	-2.76 (-6.35, 0.83)
	Treatment P-value			0.13172
	Hedge's g (95% CI)			-0.14 (-0.36, 0.09)
	Interaction P-value [b]			0.59699

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.DS.MM.S7.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Dyspnoea Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Paclitaxel	N, n	141, 115	112, 72	
	Baseline Mean (SD)	20.29 (21.94)	13.43 (19.91)	
	Change from Baseline LS Mean (SE)	2.75 (1.47)	5.15 (1.87)	-2.40 (-7.08, 2.28)
	Treatment P-value			0.31424
	Hedge's g (95% CI)			-0.12 (-0.41, 0.17)
Docetaxel	N, n	87, 65	117, 77	
	Baseline Mean (SD)	13.85 (21.16)	15.15 (20.62)	
	Change from Baseline LS Mean (SE)	3.99 (1.96)	5.46 (1.85)	-1.46 (-6.77, 3.84)
	Treatment P-value			0.58770
	Hedge's g (95% CI)			-0.08 (-0.41, 0.25)

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC.DS.MM.S7.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Dyspnoea Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Vinflunine	N, n	73, 52	78, 47	
	Baseline Mean (SD)	12.82 (19.97)	21.99 (28.89)	
	Change from Baseline LS Mean (SE)	4.72 (2.24)	8.71 (2.37)	-3.99 (-10.40, 2.43)
	Treatment P-value			0.22277
	Hedge's g (95% CI)			-0.17 (-0.56, 0.23)
	Interaction P-value [b]			0.23067

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.DS.MM.S8.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Dyspnoea Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Primary Site of Tumor

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Upper Tract	N, n	98, 75	107, 76	
	Baseline Mean (SD)	14.67 (19.17)	14.91 (20.65)	
	Change from Baseline LS Mean (SE)	4.88 (1.83)	5.65 (1.84)	-0.77 (-5.88, 4.34)
	Treatment P-value			0.76696
	Hedge's g (95% CI)			-0.04 (-0.36, 0.28)
Other	N, n	203, 157	200, 120	
	Baseline Mean (SD)	17.83 (22.50)	16.94 (24.06)	
	Change from Baseline LS Mean (SE)	2.81 (1.29)	6.44 (1.48)	-3.63 (-7.49, 0.23)
	Treatment P-value			0.06524
	Hedge's g (95% CI)			-0.18 (-0.41, 0.06)
	Interaction P-value [b]			0.30062

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.DS.MM.S9.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Dyspnoea Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
1-2 lines	N, n	262, 203	270, 169	
	Baseline Mean (SD)	17.57 (21.83)	16.57 (22.75)	
	Change from Baseline LS Mean (SE)	3.18 (1.14)	6.24 (1.25)	-3.07 (-6.38, 0.25)
	Treatment P-value			0.07012
	Hedge's g (95% CI)			-0.15 (-0.35, 0.05)
>=3 lines	N, n	39, 29	37, 27	
	Baseline Mean (SD)	11.49 (18.42)	13.58 (23.13)	
	Change from Baseline LS Mean (SE)	5.41 (2.83)	5.53 (3.11)	-0.12 (-8.39, 8.15)
	Treatment P-value			0.97751
	Hedge's g (95% CI)			-0.01 (-0.52, 0.51)
	Interaction P-value [b]			0.68589

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.DS.MM.S10.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Dyspnoea Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Best Response to Prior CPI

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Responder	N, n	61, 49	50, 34	
	Baseline Mean (SD)	14.97 (21.58)	15.69 (22.07)	
	Change from Baseline LS Mean (SE)	5.75 (2.30)	8.43 (2.80)	-2.68 (-9.79, 4.44)
	Treatment P-value			0.45964
	Hedge's g (95% CI)			-0.13 (-0.56, 0.31)
Non-responder	N, n	207, 156	215, 136	
	Baseline Mean (SD)	16.88 (21.58)	17.89 (23.63)	
	Change from Baseline LS Mean (SE)	3.55 (1.31)	5.04 (1.42)	-1.49 (-5.30, 2.31)
	Treatment P-value			0.44119
	Hedge's g (95% CI)			-0.07 (-0.30, 0.16)
	Interaction P-value [b]			0.74997

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

2.4.3.5 Schlaflosigkeit

Astellas: 7465-CL-0301
Table EORTC.SLS.MM.S1.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Insomnia Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Age Group 1

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
<65 years	N, n	108, 85	111, 68	
	Baseline Mean (SD)	25.88 (26.42)	24.51 (23.48)	
	Change from Baseline LS Mean (SE)	-0.92 (1.87)	-1.23 (2.07)	0.31 (-5.17, 5.79)
	Treatment P-value			0.91133
	Hedge's g (95% CI)			0.01 (-0.30, 0.33)
>=65 years	N, n	193, 147	196, 128	
	Baseline Mean (SD)	24.49 (27.40)	22.92 (26.70)	
	Change from Baseline LS Mean (SE)	2.53 (1.43)	7.03 (1.56)	-4.49 (-8.66, -0.33)
	Treatment P-value			0.03431
	Hedge's g (95% CI)			-0.18 (-0.42, 0.05)
	Interaction P-value [b]			0.30115

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.SLS.MM.S2.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Insomnia Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Age Group 2

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
<75 years	N, n	249, 195	239, 150	
	Baseline Mean (SD)	24.27 (26.71)	24.89 (26.25)	
	Change from Baseline LS Mean (SE)	0.67 (1.25)	2.22 (1.43)	-1.55 (-5.28, 2.17)
	Treatment P-value			0.41307
	Hedge's g (95% CI)			-0.07 (-0.28, 0.15)
>=75 years	N, n	52, 37	68, 46	
	Baseline Mean (SD)	28.83 (28.50)	18.84 (22.94)	
	Change from Baseline LS Mean (SE)	4.46 (2.92)	10.35 (2.60)	-5.90 (-13.59, 1.79)
	Treatment P-value			0.13257
	Hedge's g (95% CI)			-0.24 (-0.67, 0.19)
	Interaction P-value [b]			0.69801

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.SLS.MM.S3.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Insomnia Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Gender

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Male	N, n	238, 182	232, 150	
	Baseline Mean (SD)	23.81 (27.27)	23.78 (25.42)	
	Change from Baseline LS Mean (SE)	2.80 (1.30)	4.00 (1.44)	-1.20 (-5.01, 2.61)
	Treatment P-value			0.53733
	Hedge's g (95% CI)			-0.05 (-0.27, 0.17)
Female	N, n	63, 50	75, 46	
	Baseline Mean (SD)	29.33 (25.77)	22.46 (26.34)	
	Change from Baseline LS Mean (SE)	-4.32 (2.47)	4.29 (2.60)	-8.61 (-15.66, -1.56)
	Treatment P-value			0.01680
	Hedge's g (95% CI)			-0.38 (-0.78, 0.02)
	Interaction P-value [b]			0.66624

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.SLS.MM.S4.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Insomnia Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Region

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Western Europe	N, n	126, 90	129, 70	
	Baseline Mean (SD)	24.81 (28.07)	24.29 (28.89)	
	Change from Baseline LS Mean (SE)	0.30 (1.82)	11.17 (2.11)	-10.86 (-16.35, -5.38)
	Treatment P-value			0.00012
	Hedge's g (95% CI)			-0.44 (-0.76, -0.13)
US	N, n	43, 28	44, 24	
	Baseline Mean (SD)	22.62 (22.32)	18.06 (21.93)	
	Change from Baseline LS Mean (SE)	2.68 (3.35)	9.65 (3.55)	-6.96 (-16.56, 2.63)
	Treatment P-value			0.15437
	Hedge's g (95% CI)			-0.29 (-0.83, 0.25)

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.SLS.MM.S4.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Insomnia Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Region

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Rest of the World	N, n	132, 114	134, 102	
	Baseline Mean (SD)	25.73 (27.35)	24.18 (23.99)	
	Change from Baseline LS Mean (SE)	1.71 (1.60)	-1.72 (1.70)	3.42 (-1.17, 8.02)
	Treatment P-value			0.14343
	Hedge's g (95% CI)			0.15 (-0.12, 0.42)
	Interaction P-value [b]			0.01391

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.SLS.MM.S5.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Insomnia Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
0	N, n	120, 102	124, 92	
	Baseline Mean (SD)	18.63 (25.51)	21.74 (24.43)	
	Change from Baseline LS Mean (SE)	3.32 (1.69)	1.47 (1.79)	1.85 (-2.98, 6.69)
	Treatment P-value			0.45178
	Hedge's g (95% CI)			0.08 (-0.20, 0.36)
1	N, n	181, 130	183, 104	
	Baseline Mean (SD)	30.00 (27.17)	25.00 (26.58)	
	Change from Baseline LS Mean (SE)	-0.68 (1.54)	6.42 (1.74)	-7.10 (-11.66, -2.54)
	Treatment P-value			0.00236
	Hedge's g (95% CI)			-0.29 (-0.55, -0.03)
	Interaction P-value [b]			0.39039

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.SLS.MM.S6.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Insomnia Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Yes	N, n	93, 63	95, 52	
	Baseline Mean (SD)	29.10 (27.75)	17.95 (23.30)	
	Change from Baseline LS Mean (SE)	-1.12 (2.20)	11.37 (2.46)	-12.49 (-18.98, -6.00)
	Treatment P-value			0.00018
	Hedge's g (95% CI)			-0.49 (-0.86, -0.12)
No	N, n	208, 169	212, 144	
	Baseline Mean (SD)	23.47 (26.63)	25.46 (26.14)	
	Change from Baseline LS Mean (SE)	2.05 (1.34)	1.62 (1.46)	0.43 (-3.46, 4.33)
	Treatment P-value			0.82708
	Hedge's g (95% CI)			0.02 (-0.20, 0.24)
	Interaction P-value [b]			0.62564

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.SLS.MM.S7.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Insomnia Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Paclitaxel	N, n	141, 115	112, 72	
	Baseline Mean (SD)	27.83 (28.59)	21.30 (23.27)	
	Change from Baseline LS Mean (SE)	-0.59 (1.60)	0.54 (2.02)	-1.14 (-6.20, 3.93)
	Treatment P-value			0.65943
	Hedge's g (95% CI)			-0.05 (-0.34, 0.25)
Docetaxel	N, n	87, 65	117, 77	
	Baseline Mean (SD)	20.00 (22.67)	23.81 (24.70)	
	Change from Baseline LS Mean (SE)	4.10 (2.13)	2.69 (2.00)	1.40 (-4.34, 7.15)
	Treatment P-value			0.63112
	Hedge's g (95% CI)			0.07 (-0.26, 0.39)

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.SLS.MM.S7.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Insomnia Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Vinflunine	N, n	73, 52	78, 47	
	Baseline Mean (SD)	25.00 (27.91)	26.24 (30.25)	
	Change from Baseline LS Mean (SE)	1.79 (2.46)	12.06 (2.57)	-10.28 (-17.27, -3.29)
	Treatment P-value			0.00406
	Hedge's g (95% CI)			-0.40 (-0.80, -0.01)
	Interaction P-value [b]			0.02724

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.SLS.MM.S8.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Insomnia Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Primary Site of Tumor

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Upper Tract	N, n	98, 75	107, 76	
	Baseline Mean (SD)	26.22 (25.29)	21.93 (25.27)	
	Change from Baseline LS Mean (SE)	1.36 (2.00)	4.03 (2.00)	-2.67 (-8.23, 2.89)
	Treatment P-value			0.34612
	Hedge's g (95% CI)			-0.11 (-0.43, 0.21)
Other	N, n	203, 157	200, 120	
	Baseline Mean (SD)	24.42 (27.83)	24.44 (25.83)	
	Change from Baseline LS Mean (SE)	1.24 (1.41)	4.05 (1.62)	-2.81 (-7.02, 1.41)
	Treatment P-value			0.19123
	Hedge's g (95% CI)			-0.12 (-0.36, 0.12)
	Interaction P-value [b]			0.30528

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.SLS.MM.S9.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Insomnia Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
1-2 lines	N, n	262, 203	270, 169	
	Baseline Mean (SD)	26.44 (27.48)	23.27 (25.41)	
	Change from Baseline LS Mean (SE)	0.48 (1.24)	3.73 (1.36)	-3.25 (-6.87, 0.37)
	Treatment P-value			0.07846
	Hedge's g (95% CI)			-0.14 (-0.34, 0.07)
>=3 lines	N, n	39, 29	37, 27	
	Baseline Mean (SD)	14.94 (21.06)	24.69 (27.10)	
	Change from Baseline LS Mean (SE)	5.86 (3.10)	6.17 (3.39)	-0.31 (-9.34, 8.72)
	Treatment P-value			0.94641
	Hedge's g (95% CI)			-0.01 (-0.53, 0.50)
	Interaction P-value [b]			0.63939

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.SLS.MM.S10.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Insomnia Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Best Response to Prior CPI

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Responder	N, n	61, 49	50, 34	
	Baseline Mean (SD)	16.33 (22.69)	28.43 (26.12)	
	Change from Baseline LS Mean (SE)	10.58 (2.45)	-4.42 (2.99)	15.00 (7.39, 22.60)
	Treatment P-value			0.00012
	Hedge's g (95% CI)			0.65 (0.21, 1.10)
Non-responder	N, n	207, 156	215, 136	
	Baseline Mean (SD)	27.78 (28.04)	23.04 (26.14)	
	Change from Baseline LS Mean (SE)	-1.26 (1.41)	5.66 (1.53)	-6.92 (-11.01, -2.83)
	Treatment P-value			0.00096
	Hedge's g (95% CI)			-0.29 (-0.52, -0.06)
	Interaction P-value [b]			0.03116

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

2.4.3.6 Appetitverlust

Astellas: 7465-CL-0301
Table EORTC.APS.MM.S1.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Appetite Loss Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Age Group 1

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
<65 years	N, n	108, 85	111, 68	
	Baseline Mean (SD)	24.71 (29.17)	16.67 (21.93)	
	Change from Baseline LS Mean (SE)	3.64 (2.08)	8.00 (2.34)	-4.35 (-10.51, 1.80)
	Treatment P-value			0.16505
	Hedge's g (95% CI)			-0.17 (-0.49, 0.15)
>=65 years	N, n	193, 147	196, 128	
	Baseline Mean (SD)	19.95 (26.65)	24.22 (26.03)	
	Change from Baseline LS Mean (SE)	11.93 (1.60)	6.58 (1.74)	5.35 (0.70, 10.00)
	Treatment P-value			0.02432
	Hedge's g (95% CI)			0.21 (-0.03, 0.44)
	Interaction P-value [b]			0.36775

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.APS.MM.S2.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Appetite Loss Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Age Group 2

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
<75 years	N, n	249, 195	239, 150	
	Baseline Mean (SD)	21.54 (27.35)	20.22 (25.00)	
	Change from Baseline LS Mean (SE)	8.00 (1.39)	6.73 (1.60)	1.27 (-2.90, 5.43)
	Treatment P-value			0.55046
	Hedge's g (95% CI)			0.05 (-0.16, 0.26)
>=75 years	N, n	52, 37	68, 46	
	Baseline Mean (SD)	22.52 (29.45)	26.09 (24.25)	
	Change from Baseline LS Mean (SE)	13.89 (3.23)	8.58 (2.91)	5.31 (-3.24, 13.86)
	Treatment P-value			0.22266
	Hedge's g (95% CI)			0.20 (-0.23, 0.63)
	Interaction P-value [b]			0.87599

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.APS.MM.S3.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Appetite Loss Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Gender

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Male	N, n	238, 182	232, 150	
	Baseline Mean (SD)	18.68 (25.37)	20.22 (24.09)	
	Change from Baseline LS Mean (SE)	10.37 (1.44)	6.80 (1.61)	3.57 (-0.68, 7.81)
	Treatment P-value			0.09972
	Hedge's g (95% CI)			0.14 (-0.08, 0.35)
Female	N, n	63, 50	75, 46	
	Baseline Mean (SD)	32.67 (32.64)	26.09 (27.14)	
	Change from Baseline LS Mean (SE)	3.38 (2.76)	8.29 (2.91)	-4.91 (-12.78, 2.97)
	Treatment P-value			0.22154
	Hedge's g (95% CI)			-0.20 (-0.59, 0.20)
	Interaction P-value [b]			0.13554

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.APS.MM.S4.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Appetite Loss Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Region

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Western Europe	N, n	126, 90	129, 70	
	Baseline Mean (SD)	18.52 (24.54)	23.81 (29.02)	
	Change from Baseline LS Mean (SE)	6.33 (2.04)	11.68 (2.36)	-5.35 (-11.49, 0.78)
	Treatment P-value			0.08696
	Hedge's g (95% CI)			-0.20 (-0.51, 0.12)
US	N, n	43, 28	44, 24	
	Baseline Mean (SD)	26.19 (30.57)	22.22 (23.40)	
	Change from Baseline LS Mean (SE)	4.48 (3.72)	5.41 (3.98)	-0.93 (-11.64, 9.78)
	Treatment P-value			0.86442
	Hedge's g (95% CI)			-0.04 (-0.57, 0.50)

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.APS.MM.S4.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Appetite Loss Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Region

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Rest of the World	N, n	132, 114	134, 102	
	Baseline Mean (SD)	23.10 (29.12)	19.93 (22.13)	
	Change from Baseline LS Mean (SE)	11.63 (1.79)	4.66 (1.91)	6.97 (1.83, 12.12)
	Treatment P-value			0.00805
	Hedge's g (95% CI)			0.28 (0.02, 0.55)
	Interaction P-value [b]			0.01069

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.APS.MM.S5.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Appetite Loss Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
0	N, n	120, 102	124, 92	
	Baseline Mean (SD)	14.05 (21.72)	17.39 (21.81)	
	Change from Baseline LS Mean (SE)	11.10 (1.89)	5.94 (2.01)	5.16 (-0.26, 10.58)
	Treatment P-value			0.06217
	Hedge's g (95% CI)			0.22 (-0.06, 0.51)
1	N, n	181, 130	183, 104	
	Baseline Mean (SD)	27.69 (30.26)	25.32 (26.88)	
	Change from Baseline LS Mean (SE)	6.82 (1.72)	8.21 (1.95)	-1.40 (-6.49, 3.70)
	Treatment P-value			0.59093
	Hedge's g (95% CI)			-0.05 (-0.31, 0.21)
	Interaction P-value [b]			0.37361

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.APS.MM.S6.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Appetite Loss Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Yes	N, n	93, 63	95, 52	
	Baseline Mean (SD)	32.28 (32.22)	28.21 (26.72)	
	Change from Baseline LS Mean (SE)	0.52 (2.45)	6.12 (2.76)	-5.60 (-12.86, 1.65)
	Treatment P-value			0.12990
	Hedge's g (95% CI)			-0.20 (-0.56, 0.17)
No	N, n	208, 169	212, 144	
	Baseline Mean (SD)	17.75 (24.68)	19.21 (23.84)	
	Change from Baseline LS Mean (SE)	11.79 (1.50)	7.46 (1.64)	4.32 (-0.03, 8.68)
	Treatment P-value			0.05170
	Hedge's g (95% CI)			0.17 (-0.05, 0.40)
	Interaction P-value [b]			0.46051

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.APS.MM.S7.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Appetite Loss Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Paclitaxel	N, n	141, 115	112, 72	
	Baseline Mean (SD)	22.03 (28.23)	19.91 (23.51)	
	Change from Baseline LS Mean (SE)	10.70 (1.77)	3.19 (2.24)	7.51 (1.90, 13.11)
	Treatment P-value			0.00881
	Hedge's g (95% CI)			0.30 (0.00, 0.59)
Docetaxel	N, n	87, 65	117, 77	
	Baseline Mean (SD)	21.03 (27.37)	20.35 (21.73)	
	Change from Baseline LS Mean (SE)	6.02 (2.35)	6.66 (2.21)	-0.64 (-6.99, 5.70)
	Treatment P-value			0.84202
	Hedge's g (95% CI)			-0.03 (-0.36, 0.30)

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.APS.MM.S7.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Appetite Loss Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Vinflunine	N, n	73, 52	78, 47	
	Baseline Mean (SD)	21.79 (27.12)	26.24 (31.03)	
	Change from Baseline LS Mean (SE)	8.20 (2.69)	14.38 (2.86)	-6.18 (-13.90, 1.54)
	Treatment P-value			0.11646
	Hedge's g (95% CI)			-0.21 (-0.60, 0.19)
	Interaction P-value [b]			0.00632

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.APS.MM.S8.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Appetite Loss Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Primary Site of Tumor

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Upper Tract	N, n	98, 75	107, 76	
	Baseline Mean (SD)	29.33 (31.93)	19.74 (24.45)	
	Change from Baseline LS Mean (SE)	4.20 (2.23)	6.92 (2.24)	-2.73 (-8.93, 3.48)
	Treatment P-value			0.38791
	Hedge's g (95% CI)			-0.11 (-0.42, 0.21)
Other	N, n	203, 157	200, 120	
	Baseline Mean (SD)	18.05 (24.60)	22.78 (25.19)	
	Change from Baseline LS Mean (SE)	11.23 (1.56)	7.30 (1.81)	3.93 (-0.76, 8.63)
	Treatment P-value			0.10028
	Hedge's g (95% CI)			0.15 (-0.09, 0.39)
	Interaction P-value [b]			0.97489

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.APS.MM.S9.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Appetite Loss Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
1-2 lines	N, n	262, 203	270, 169	
	Baseline Mean (SD)	22.00 (28.10)	20.71 (24.90)	
	Change from Baseline LS Mean (SE)	8.52 (1.38)	8.06 (1.52)	0.46 (-3.56, 4.49)
	Treatment P-value			0.82055
	Hedge's g (95% CI)			0.02 (-0.19, 0.22)
>=3 lines	N, n	39, 29	37, 27	
	Baseline Mean (SD)	19.54 (24.43)	27.16 (24.52)	
	Change from Baseline LS Mean (SE)	11.11 (3.45)	1.50 (3.76)	9.62 (-0.42, 19.65)
	Treatment P-value			0.06033
	Hedge's g (95% CI)			0.39 (-0.13, 0.91)
	Interaction P-value [b]			0.23334

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.APS.MM.S10.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Appetite Loss Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Best Response to Prior CPI

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Responder	N, n	61, 49	50, 34	
	Baseline Mean (SD)	13.61 (20.32)	24.51 (20.61)	
	Change from Baseline LS Mean (SE)	13.83 (2.75)	2.52 (3.36)	11.31 (2.78, 19.84)
	Treatment P-value			0.00952
	Hedge's g (95% CI)			0.44 (0.00, 0.88)
Non-responder	N, n	207, 156	215, 136	
	Baseline Mean (SD)	22.86 (28.54)	21.81 (26.41)	
	Change from Baseline LS Mean (SE)	8.41 (1.57)	8.13 (1.71)	0.28 (-4.28, 4.84)
	Treatment P-value			0.90388
	Hedge's g (95% CI)			0.01 (-0.22, 0.24)
	Interaction P-value [b]			0.66366

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

2.4.3.7 Obstipation

Astellas: 7465-CL-0301
Table EORTC.COS.MM.S1.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Constipation Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Age Group 1

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
<65 years	N, n	108, 85	111, 68	
	Baseline Mean (SD)	21.96 (28.43)	15.20 (24.05)	
	Change from Baseline LS Mean (SE)	-0.98 (1.78)	0.71 (1.98)	-1.68 (-6.93, 3.56)
	Treatment P-value			0.52851
	Hedge's g (95% CI)			-0.08 (-0.39, 0.24)
>=65 years	N, n	193, 147	196, 128	
	Baseline Mean (SD)	19.95 (25.78)	21.61 (28.55)	
	Change from Baseline LS Mean (SE)	-0.43 (1.37)	1.46 (1.50)	-1.89 (-5.89, 2.11)
	Treatment P-value			0.35316
	Hedge's g (95% CI)			-0.08 (-0.32, 0.15)
	Interaction P-value [b]			0.54754

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.COS.MM.S2.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Constipation Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Age Group 2

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
<75 years	N, n	249, 195	239, 150	
	Baseline Mean (SD)	20.85 (27.25)	19.56 (28.16)	
	Change from Baseline LS Mean (SE)	-0.13 (1.20)	0.69 (1.37)	-0.82 (-4.40, 2.76)
	Treatment P-value			0.65277
	Hedge's g (95% CI)			-0.04 (-0.25, 0.18)
>=75 years	N, n	52, 37	68, 46	
	Baseline Mean (SD)	19.82 (24.16)	18.84 (23.99)	
	Change from Baseline LS Mean (SE)	-3.64 (2.77)	3.01 (2.47)	-6.65 (-13.96, 0.65)
	Treatment P-value			0.07390
	Hedge's g (95% CI)			-0.28 (-0.72, 0.15)
	Interaction P-value [b]			0.32877

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.COS.MM.S3.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Constipation Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Gender

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Male	N, n	238, 182	232, 150	
	Baseline Mean (SD)	19.23 (26.27)	20.67 (27.76)	
	Change from Baseline LS Mean (SE)	-0.88 (1.24)	1.08 (1.38)	-1.96 (-5.60, 1.68)
	Treatment P-value			0.29045
	Hedge's g (95% CI)			-0.09 (-0.30, 0.13)
Female	N, n	63, 50	75, 46	
	Baseline Mean (SD)	26.00 (28.00)	15.22 (25.05)	
	Change from Baseline LS Mean (SE)	0.29 (2.33)	1.84 (2.46)	-1.56 (-8.21, 5.10)
	Treatment P-value			0.64605
	Hedge's g (95% CI)			-0.07 (-0.47, 0.32)
	Interaction P-value [b]			0.09503

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.COS.MM.S4.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Constipation Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Region

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Western Europe	N, n	126, 90	129, 70	
	Baseline Mean (SD)	18.52 (26.96)	22.38 (29.88)	
	Change from Baseline LS Mean (SE)	1.75 (1.72)	7.21 (2.00)	-5.46 (-10.63, -0.28)
	Treatment P-value			0.03891
	Hedge's g (95% CI)			-0.22 (-0.53, 0.09)
US	N, n	43, 28	44, 24	
	Baseline Mean (SD)	15.48 (23.10)	11.11 (16.05)	
	Change from Baseline LS Mean (SE)	2.89 (3.13)	5.65 (3.35)	-2.76 (-11.77, 6.25)
	Treatment P-value			0.54720
	Hedge's g (95% CI)			-0.13 (-0.67, 0.40)

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.COS.MM.S4.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Constipation Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Region

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Rest of the World	N, n	132, 114	134, 102	
	Baseline Mean (SD)	23.68 (27.24)	19.28 (27.12)	
	Change from Baseline LS Mean (SE)	-3.03 (1.51)	-3.63 (1.61)	0.60 (-3.75, 4.95)
	Treatment P-value			0.78640
	Hedge's g (95% CI)			0.03 (-0.24, 0.30)
	Interaction P-value [b]			0.03004

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.COS.MM.S5.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Constipation Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
0	N, n	120, 102	124, 92	
	Baseline Mean (SD)	17.97 (25.55)	14.13 (22.77)	
	Change from Baseline LS Mean (SE)	-0.41 (1.59)	0.47 (1.70)	-0.88 (-5.45, 3.70)
	Treatment P-value			0.70671
	Hedge's g (95% CI)			-0.04 (-0.33, 0.24)
1	N, n	181, 130	183, 104	
	Baseline Mean (SD)	22.82 (27.54)	24.04 (29.91)	
	Change from Baseline LS Mean (SE)	-0.94 (1.46)	1.70 (1.65)	-2.64 (-6.97, 1.69)
	Treatment P-value			0.23187
	Hedge's g (95% CI)			-0.11 (-0.36, 0.15)
	Interaction P-value [b]			0.27330

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.COS.MM.S6.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Constipation Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Yes	N, n	93, 63	95, 52	
	Baseline Mean (SD)	30.16 (30.94)	20.51 (28.89)	
	Change from Baseline LS Mean (SE)	-10.43 (2.07)	4.78 (2.36)	-15.21 (-21.38, -9.04)
	Treatment P-value			<.00001
	Hedge's g (95% CI)			-0.63 (-1.00, -0.25)
No	N, n	208, 169	212, 144	
	Baseline Mean (SD)	17.16 (24.15)	18.98 (26.64)	
	Change from Baseline LS Mean (SE)	2.82 (1.28)	-0.02 (1.39)	2.84 (-0.87, 6.56)
	Treatment P-value			0.13295
	Hedge's g (95% CI)			0.13 (-0.09, 0.35)
	Interaction P-value [b]			0.01556

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.COS.MM.S7.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Constipation Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Paclitaxel	N, n	141, 115	112, 72	
	Baseline Mean (SD)	21.74 (27.59)	16.20 (26.83)	
	Change from Baseline LS Mean (SE)	-0.47 (1.49)	1.63 (1.87)	-2.11 (-6.80, 2.59)
	Treatment P-value			0.37872
	Hedge's g (95% CI)			-0.10 (-0.39, 0.20)
Docetaxel	N, n	87, 65	117, 77	
	Baseline Mean (SD)	20.51 (24.07)	17.75 (24.53)	
	Change from Baseline LS Mean (SE)	-2.48 (1.96)	-3.65 (1.88)	1.17 (-4.16, 6.51)
	Treatment P-value			0.66570
	Hedge's g (95% CI)			0.06 (-0.27, 0.39)

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.COS.MM.S7.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Constipation Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Vinflunine	N, n	73, 52	78, 47	
	Baseline Mean (SD)	18.59 (28.33)	26.95 (30.80)	
	Change from Baseline LS Mean (SE)	1.55 (2.27)	8.26 (2.36)	-6.71 (-13.15, -0.27)
	Treatment P-value			0.04104
	Hedge's g (95% CI)			-0.25 (-0.64, 0.15)
	Interaction P-value [b]			0.00307

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.COS.MM.S8.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Constipation Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Primary Site of Tumor

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Upper Tract	N, n	98, 75	107, 76	
	Baseline Mean (SD)	28.44 (28.84)	17.98 (28.51)	
	Change from Baseline LS Mean (SE)	-5.64 (1.88)	4.18 (1.90)	-9.82 (-15.07, -4.58)
	Treatment P-value			0.00026
	Hedge's g (95% CI)			-0.42 (-0.74, -0.10)
Other	N, n	203, 157	200, 120	
	Baseline Mean (SD)	16.99 (24.93)	20.28 (26.39)	
	Change from Baseline LS Mean (SE)	1.90 (1.34)	-0.76 (1.54)	2.65 (-1.35, 6.66)
	Treatment P-value			0.19351
	Hedge's g (95% CI)			0.12 (-0.11, 0.36)
	Interaction P-value [b]			0.14473

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.COS.MM.S9.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Constipation Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
1-2 lines	N, n	262, 203	270, 169	
	Baseline Mean (SD)	21.35 (26.82)	17.95 (27.22)	
	Change from Baseline LS Mean (SE)	-0.96 (1.19)	2.03 (1.30)	-2.99 (-6.46, 0.47)
	Treatment P-value			0.09003
	Hedge's g (95% CI)			-0.13 (-0.34, 0.07)
>=3 lines	N, n	39, 29	37, 27	
	Baseline Mean (SD)	16.09 (26.16)	28.40 (25.66)	
	Change from Baseline LS Mean (SE)	1.23 (2.87)	-3.96 (3.21)	5.19 (-3.27, 13.66)
	Treatment P-value			0.22867
	Hedge's g (95% CI)			0.25 (-0.27, 0.77)
	Interaction P-value [b]			0.76220

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.COS.MM.S10.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Constipation Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Best Response to Prior CPI

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Responder	N, n	61, 49	50, 34	
	Baseline Mean (SD)	14.97 (21.58)	15.69 (24.94)	
	Change from Baseline LS Mean (SE)	3.09 (2.34)	3.82 (2.84)	-0.73 (-7.97, 6.52)
	Treatment P-value			0.84378
	Hedge's g (95% CI)			-0.03 (-0.47, 0.40)
Non-responder	N, n	207, 156	215, 136	
	Baseline Mean (SD)	22.44 (27.61)	20.59 (27.53)	
	Change from Baseline LS Mean (SE)	-1.43 (1.36)	0.59 (1.48)	-2.02 (-5.98, 1.94)
	Treatment P-value			0.31586
	Hedge's g (95% CI)			-0.09 (-0.32, 0.14)
	Interaction P-value [b]			0.82248

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

2.4.3.8 Diarrhö

Astellas: 7465-CL-0301
Table EORTC.DIS.MM.S1.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Diarrhoea Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Age Group 1

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
<65 years	N, n	108, 85	111, 68	
	Baseline Mean (SD)	6.67 (14.36)	9.31 (18.97)	
	Change from Baseline LS Mean (SE)	5.83 (1.53)	1.84 (1.72)	3.98 (-0.55, 8.51)
	Treatment P-value			0.08461
	Hedge's g (95% CI)			0.21 (-0.11, 0.52)
>=65 years	N, n	193, 147	196, 128	
	Baseline Mean (SD)	6.80 (16.52)	5.21 (15.33)	
	Change from Baseline LS Mean (SE)	6.94 (1.18)	4.76 (1.29)	2.18 (-1.26, 5.61)
	Treatment P-value			0.21309
	Hedge's g (95% CI)			0.10 (-0.13, 0.34)
	Interaction P-value [b]			0.74606

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.DIS.MM.S2.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Diarrhoea Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Age Group 2

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
<75 years	N, n	249, 195	239, 150	
	Baseline Mean (SD)	6.32 (14.36)	6.67 (17.27)	
	Change from Baseline LS Mean (SE)	7.24 (1.02)	3.59 (1.18)	3.65 (0.58, 6.72)
	Treatment P-value			0.01974
	Hedge's g (95% CI)			0.18 (-0.03, 0.39)
>=75 years	N, n	52, 37	68, 46	
	Baseline Mean (SD)	9.01 (21.73)	6.52 (15.10)	
	Change from Baseline LS Mean (SE)	2.18 (2.38)	3.94 (2.13)	-1.76 (-8.03, 4.52)
	Treatment P-value			0.58259
	Hedge's g (95% CI)			-0.08 (-0.51, 0.35)
	Interaction P-value [b]			0.84725

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.DIS.MM.S3.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Diarrhoea Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Gender

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Male	N, n	238, 182	232, 150	
	Baseline Mean (SD)	6.59 (15.84)	5.56 (14.66)	
	Change from Baseline LS Mean (SE)	7.02 (1.06)	4.32 (1.18)	2.71 (-0.41, 5.82)
	Treatment P-value			0.08824
	Hedge's g (95% CI)			0.13 (-0.09, 0.35)
Female	N, n	63, 50	75, 46	
	Baseline Mean (SD)	7.33 (15.49)	10.14 (22.08)	
	Change from Baseline LS Mean (SE)	4.67 (2.02)	1.40 (2.13)	3.27 (-2.49, 9.03)
	Treatment P-value			0.26559
	Hedge's g (95% CI)			0.18 (-0.22, 0.57)
	Interaction P-value [b]			0.31774

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.DIS.MM.S4.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Diarrhoea Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Region

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Western Europe	N, n	126, 90	129, 70	
	Baseline Mean (SD)	5.93 (17.00)	6.67 (18.48)	
	Change from Baseline LS Mean (SE)	6.86 (1.49)	3.14 (1.74)	3.73 (-0.78, 8.24)
	Treatment P-value			0.10490
	Hedge's g (95% CI)			0.16 (-0.15, 0.48)
US	N, n	43, 28	44, 24	
	Baseline Mean (SD)	10.71 (18.27)	2.78 (9.41)	
	Change from Baseline LS Mean (SE)	3.70 (2.73)	10.46 (2.87)	-6.76 (-14.55, 1.02)
	Treatment P-value			0.08852
	Hedge's g (95% CI)			-0.32 (-0.86, 0.22)

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.DIS.MM.S4.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Diarrhoea Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Region

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Rest of the World	N, n	132, 114	134, 102	
	Baseline Mean (SD)	6.43 (13.94)	7.52 (16.85)	
	Change from Baseline LS Mean (SE)	6.71 (1.32)	2.46 (1.41)	4.25 (0.45, 8.04)
	Treatment P-value			0.02842
	Hedge's g (95% CI)			0.23 (-0.04, 0.50)
	Interaction P-value [b]			0.68880

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.DIS.MM.S5.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Diarrhoea Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
0	N, n	120, 102	124, 92	
	Baseline Mean (SD)	5.23 (12.18)	6.52 (17.29)	
	Change from Baseline LS Mean (SE)	5.56 (1.37)	1.89 (1.47)	3.67 (-0.29, 7.62)
	Treatment P-value			0.06896
	Hedge's g (95% CI)			0.21 (-0.08, 0.49)
1	N, n	181, 130	183, 104	
	Baseline Mean (SD)	7.95 (18.00)	6.73 (16.34)	
	Change from Baseline LS Mean (SE)	7.27 (1.26)	5.36 (1.42)	1.91 (-1.82, 5.64)
	Treatment P-value			0.31405
	Hedge's g (95% CI)			0.09 (-0.17, 0.34)
	Interaction P-value [b]			0.74276

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.DIS.MM.S6.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Diarrhoea Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Yes	N, n	93, 63	95, 52	
	Baseline Mean (SD)	7.41 (18.40)	6.41 (16.22)	
	Change from Baseline LS Mean (SE)	4.80 (1.79)	5.59 (2.02)	-0.79 (-6.10, 4.51)
	Treatment P-value			0.76863
	Hedge's g (95% CI)			-0.04 (-0.40, 0.33)
No	N, n	208, 169	212, 144	
	Baseline Mean (SD)	6.51 (14.67)	6.71 (16.99)	
	Change from Baseline LS Mean (SE)	7.12 (1.10)	2.98 (1.20)	4.14 (0.94, 7.34)
	Treatment P-value			0.01128
	Hedge's g (95% CI)			0.21 (-0.01, 0.43)
	Interaction P-value [b]			0.41335

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.DIS.MM.S7.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Diarrhoea Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Paclitaxel	N, n	141, 115	112, 72	
	Baseline Mean (SD)	5.51 (14.60)	4.17 (15.76)	
	Change from Baseline LS Mean (SE)	9.21 (1.29)	1.82 (1.63)	7.40 (3.31, 11.48)
	Treatment P-value			0.00042
	Hedge's g (95% CI)			0.39 (0.09, 0.68)
Docetaxel	N, n	87, 65	117, 77	
	Baseline Mean (SD)	9.23 (16.15)	9.52 (18.62)	
	Change from Baseline LS Mean (SE)	2.26 (1.71)	6.23 (1.61)	-3.97 (-8.59, 0.65)
	Treatment P-value			0.09216
	Hedge's g (95% CI)			-0.20 (-0.53, 0.13)

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.DIS.MM.S7.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Diarrhoea Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Vinflunine	N, n	73, 52	78, 47	
	Baseline Mean (SD)	6.41 (17.51)	5.67 (14.44)	
	Change from Baseline LS Mean (SE)	5.72 (1.97)	2.48 (2.09)	3.24 (-2.40, 8.88)
	Treatment P-value			0.25982
	Hedge's g (95% CI)			0.14 (-0.25, 0.54)
	Interaction P-value [b]			0.00033

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.DIS.MM.S8.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Diarrhoea Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Primary Site of Tumor

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Upper Tract	N, n	98, 75	107, 76	
	Baseline Mean (SD)	6.22 (13.08)	7.02 (19.10)	
	Change from Baseline LS Mean (SE)	7.34 (1.62)	0.92 (1.62)	6.42 (1.92, 10.92)
	Treatment P-value			0.00529
	Hedge's g (95% CI)			0.32 (0.00, 0.64)
Other	N, n	203, 157	200, 120	
	Baseline Mean (SD)	7.01 (16.89)	6.39 (15.15)	
	Change from Baseline LS Mean (SE)	6.11 (1.14)	5.45 (1.32)	0.66 (-2.76, 4.09)
	Treatment P-value			0.70320
	Hedge's g (95% CI)			0.03 (-0.20, 0.27)
	Interaction P-value [b]			0.07055

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.DIS.MM.S9.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Diarrhoea Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
1-2 lines	N, n	262, 203	270, 169	
	Baseline Mean (SD)	7.06 (16.23)	6.51 (15.97)	
	Change from Baseline LS Mean (SE)	6.42 (1.02)	4.09 (1.12)	2.33 (-0.64, 5.29)
	Treatment P-value			0.12360
	Hedge's g (95% CI)			0.11 (-0.09, 0.32)
>=3 lines	N, n	39, 29	37, 27	
	Baseline Mean (SD)	4.60 (11.70)	7.41 (21.35)	
	Change from Baseline LS Mean (SE)	7.10 (2.49)	0.92 (2.74)	6.18 (-1.10, 13.45)
	Treatment P-value			0.09578
	Hedge's g (95% CI)			0.31 (-0.21, 0.83)
	Interaction P-value [b]			0.80728

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.DIS.MM.S10.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Diarrhoea Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Best Response to Prior CPI

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Responder	N, n	61, 49	50, 34	
	Baseline Mean (SD)	3.40 (10.19)	9.80 (20.97)	
	Change from Baseline LS Mean (SE)	7.40 (1.91)	-0.83 (2.32)	8.23 (2.33, 14.13)
	Treatment P-value			0.00642
	Hedge's g (95% CI)			0.39 (-0.05, 0.83)
Non-responder	N, n	207, 156	215, 136	
	Baseline Mean (SD)	7.48 (16.75)	6.13 (15.82)	
	Change from Baseline LS Mean (SE)	6.27 (1.12)	3.90 (1.23)	2.37 (-0.90, 5.64)
	Treatment P-value			0.15422
	Hedge's g (95% CI)			0.12 (-0.11, 0.35)
	Interaction P-value [b]			0.44378

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

2.4.3.9 Finanzielle Schwierigkeiten

Astellas: 7465-CL-0301
Table EORTC.FIS.MM.S1.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Financial Difficulties Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Age Group 1

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
<65 years	N, n	108, 85	111, 68	
	Baseline Mean (SD)	16.08 (22.78)	17.16 (23.39)	
	Change from Baseline LS Mean (SE)	0.70 (1.34)	0.45 (1.50)	0.25 (-3.71, 4.20)
	Treatment P-value			0.90150
	Hedge's g (95% CI)			0.01 (-0.30, 0.33)
>=65 years	N, n	193, 147	196, 128	
	Baseline Mean (SD)	9.52 (19.89)	8.85 (18.46)	
	Change from Baseline LS Mean (SE)	0.12 (1.03)	2.44 (1.11)	-2.32 (-5.30, 0.66)
	Treatment P-value			0.12628
	Hedge's g (95% CI)			-0.15 (-0.39, 0.08)
	Interaction P-value [b]			0.30104

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.FIS.MM.S2.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Financial Difficulties Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Age Group 2

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
<75 years	N, n	249, 195	239, 150	
	Baseline Mean (SD)	12.82 (22.21)	13.11 (21.81)	
	Change from Baseline LS Mean (SE)	0.31 (0.89)	1.49 (1.02)	-1.18 (-3.84, 1.48)
	Treatment P-value			0.38258
	Hedge's g (95% CI)			-0.07 (-0.28, 0.14)
>=75 years	N, n	52, 37	68, 46	
	Baseline Mean (SD)	7.21 (13.91)	7.25 (15.58)	
	Change from Baseline LS Mean (SE)	0.56 (2.10)	2.41 (1.87)	-1.85 (-7.39, 3.68)
	Treatment P-value			0.51048
	Hedge's g (95% CI)			-0.13 (-0.55, 0.30)
	Interaction P-value [b]			0.84180

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC.FIS.MM.S3.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Financial Difficulties Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Gender

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Male	N, n	238, 182	232, 150	
	Baseline Mean (SD)	11.90 (21.28)	11.78 (19.74)	
	Change from Baseline LS Mean (SE)	0.19 (0.93)	1.94 (1.02)	-1.74 (-4.46, 0.97)
	Treatment P-value			0.20702
	Hedge's g (95% CI)			-0.10 (-0.32, 0.11)
Female	N, n	63, 50	75, 46	
	Baseline Mean (SD)	12.00 (21.04)	11.59 (23.54)	
	Change from Baseline LS Mean (SE)	0.78 (1.77)	0.87 (1.86)	-0.09 (-5.14, 4.96)
	Treatment P-value			0.97240
	Hedge's g (95% CI)			-0.01 (-0.40, 0.39)
	Interaction P-value [b]			0.54254

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.FIS.MM.S4.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Financial Difficulties Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Region

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Western Europe	N, n	126, 90	129, 70	
	Baseline Mean (SD)	7.41 (16.40)	7.62 (21.36)	
	Change from Baseline LS Mean (SE)	1.20 (1.32)	3.29 (1.52)	-2.08 (-6.04, 1.87)
	Treatment P-value			0.30130
	Hedge's g (95% CI)			-0.14 (-0.45, 0.17)
US	N, n	43, 28	44, 24	
	Baseline Mean (SD)	13.10 (26.20)	13.89 (23.91)	
	Change from Baseline LS Mean (SE)	-0.05 (2.45)	1.06 (2.56)	-1.11 (-8.08, 5.86)
	Treatment P-value			0.75365
	Hedge's g (95% CI)			-0.06 (-0.60, 0.47)

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.FIS.MM.S4.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Financial Difficulties Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Region

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Rest of the World	N, n	132, 114	134, 102	
	Baseline Mean (SD)	15.20 (22.67)	14.05 (19.02)	
	Change from Baseline LS Mean (SE)	-0.24 (1.16)	0.85 (1.23)	-1.10 (-4.43, 2.24)
	Treatment P-value			0.51788
	Hedge's g (95% CI)			-0.06 (-0.33, 0.20)
	Interaction P-value [b]			0.91663

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC.FIS.MM.S5.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Financial Difficulties Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
0	N, n	120, 102	124, 92	
	Baseline Mean (SD)	9.15 (19.43)	11.96 (20.72)	
	Change from Baseline LS Mean (SE)	0.62 (1.22)	0.97 (1.29)	-0.34 (-3.84, 3.15)
	Treatment P-value			0.84727
	Hedge's g (95% CI)			-0.02 (-0.30, 0.26)
1	N, n	181, 130	183, 104	
	Baseline Mean (SD)	14.10 (22.30)	11.54 (20.65)	
	Change from Baseline LS Mean (SE)	0.02 (1.11)	2.40 (1.25)	-2.38 (-5.66, 0.89)
	Treatment P-value			0.15355
	Hedge's g (95% CI)			-0.14 (-0.40, 0.11)
	Interaction P-value [b]			0.91341

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC.FIS.MM.S6.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Financial Difficulties Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Yes	N, n	93, 63	95, 52	
	Baseline Mean (SD)	11.64 (21.72)	7.69 (15.64)	
	Change from Baseline LS Mean (SE)	0.98 (1.58)	2.51 (1.75)	-1.54 (-6.17, 3.10)
	Treatment P-value			0.51557
	Hedge's g (95% CI)			-0.09 (-0.46, 0.27)
No	N, n	208, 169	212, 144	
	Baseline Mean (SD)	12.03 (21.05)	13.19 (22.03)	
	Change from Baseline LS Mean (SE)	0.07 (0.96)	1.46 (1.04)	-1.39 (-4.17, 1.40)
	Treatment P-value			0.32755
	Hedge's g (95% CI)			-0.09 (-0.31, 0.14)
	Interaction P-value [b]			0.37846

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
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Astellas: 7465-CL-0301
Table EORTC.FIS.MM.S7.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Financial Difficulties Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Paclitaxel	N, n	141, 115	112, 72	
	Baseline Mean (SD)	15.65 (24.31)	12.50 (21.98)	
	Change from Baseline LS Mean (SE)	-0.06 (1.16)	1.88 (1.46)	-1.95 (-5.60, 1.71)
	Treatment P-value			0.29619
	Hedge's g (95% CI)			-0.11 (-0.40, 0.18)
Docetaxel	N, n	87, 65	117, 77	
	Baseline Mean (SD)	8.21 (16.70)	14.29 (21.24)	
	Change from Baseline LS Mean (SE)	1.99 (1.55)	-0.15 (1.44)	2.14 (-2.01, 6.30)
	Treatment P-value			0.31164
	Hedge's g (95% CI)			0.14 (-0.19, 0.47)

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.FIS.MM.S7.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Financial Difficulties Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Vinflunine	N, n	73, 52	78, 47	
	Baseline Mean (SD)	8.33 (17.31)	6.38 (16.50)	
	Change from Baseline LS Mean (SE)	-0.93 (1.77)	4.56 (1.86)	-5.49 (-10.53, -0.45)
	Treatment P-value			0.03283
	Hedge's g (95% CI)			-0.36 (-0.76, 0.03)
	Interaction P-value [b]			0.41680

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.FIS.MM.S8.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Financial Difficulties Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Primary Site of Tumor

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Upper Tract	N, n	98, 75	107, 76	
	Baseline Mean (SD)	16.89 (25.33)	9.65 (20.23)	
	Change from Baseline LS Mean (SE)	-1.34 (1.43)	0.25 (1.42)	-1.59 (-5.56, 2.38)
	Treatment P-value			0.43222
	Hedge's g (95% CI)			-0.10 (-0.42, 0.21)
Other	N, n	203, 157	200, 120	
	Baseline Mean (SD)	9.55 (18.51)	13.06 (20.86)	
	Change from Baseline LS Mean (SE)	1.16 (1.00)	2.60 (1.15)	-1.44 (-4.43, 1.54)
	Treatment P-value			0.34275
	Hedge's g (95% CI)			-0.09 (-0.32, 0.15)
	Interaction P-value [b]			0.18818

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.FIS.MM.S9.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Financial Difficulties Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
1-2 lines	N, n	262, 203	270, 169	
	Baseline Mean (SD)	12.32 (21.66)	11.24 (19.88)	
	Change from Baseline LS Mean (SE)	0.07 (0.88)	1.33 (0.96)	-1.26 (-3.82, 1.31)
	Treatment P-value			0.33518
	Hedge's g (95% CI)			-0.08 (-0.28, 0.12)
>=3 lines	N, n	39, 29	37, 27	
	Baseline Mean (SD)	9.20 (17.59)	14.81 (25.04)	
	Change from Baseline LS Mean (SE)	1.89 (2.23)	3.97 (2.42)	-2.08 (-8.54, 4.39)
	Treatment P-value			0.52814
	Hedge's g (95% CI)			-0.11 (-0.63, 0.41)
	Interaction P-value [b]			0.49893

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.FIS.MM.S10.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Financial Difficulties Symptom Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Best Response to Prior CPI

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Responder	N, n	61, 49	50, 34	
	Baseline Mean (SD)	11.56 (18.70)	9.80 (19.30)	
	Change from Baseline LS Mean (SE)	1.24 (1.80)	5.96 (2.19)	-4.72 (-10.29, 0.85)
	Treatment P-value			0.09646
	Hedge's g (95% CI)			-0.28 (-0.72, 0.15)
Non-responder	N, n	207, 156	215, 136	
	Baseline Mean (SD)	12.18 (21.78)	12.75 (21.87)	
	Change from Baseline LS Mean (SE)	0.55 (1.02)	0.46 (1.11)	0.09 (-2.88, 3.07)
	Treatment P-value			0.95078
	Hedge's g (95% CI)			0.01 (-0.22, 0.23)
	Interaction P-value [b]			0.26940

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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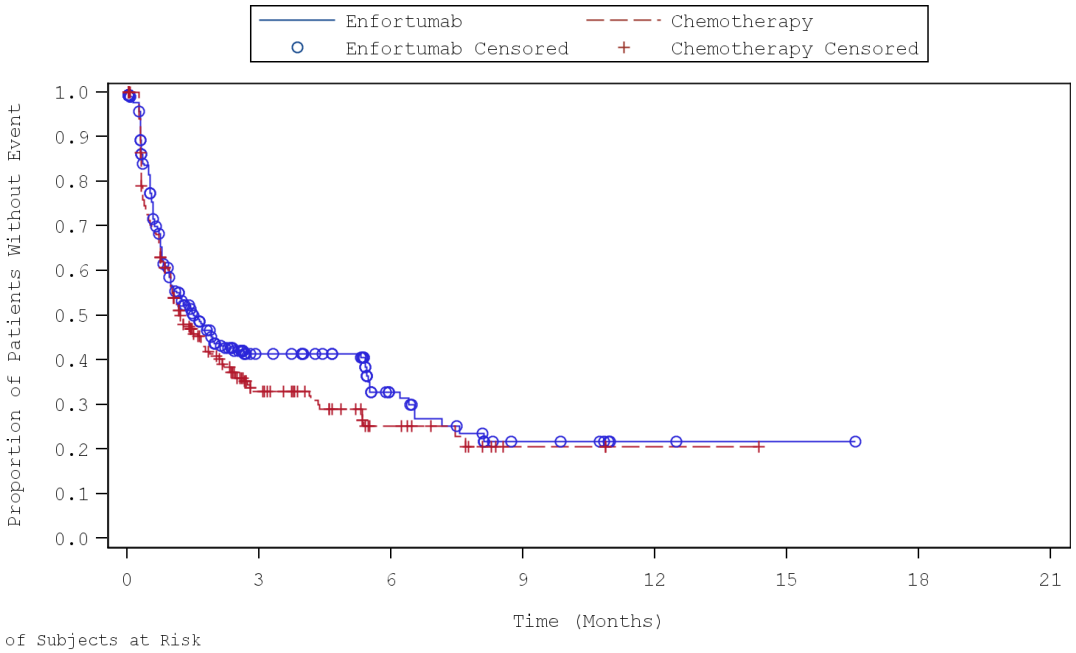
Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

2.5 Kaplan-Meier Kurven zur Symptomatik anhand des EORTC QLQ-C30 – Sensitivitätsanalyse (Responderschwelle ≥ 15 Punkte)

Astellas: 7465-CL-0301
Figure EORTC15.FS.KM.FAS: EORTC Fatigue Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Overall, Level: NA



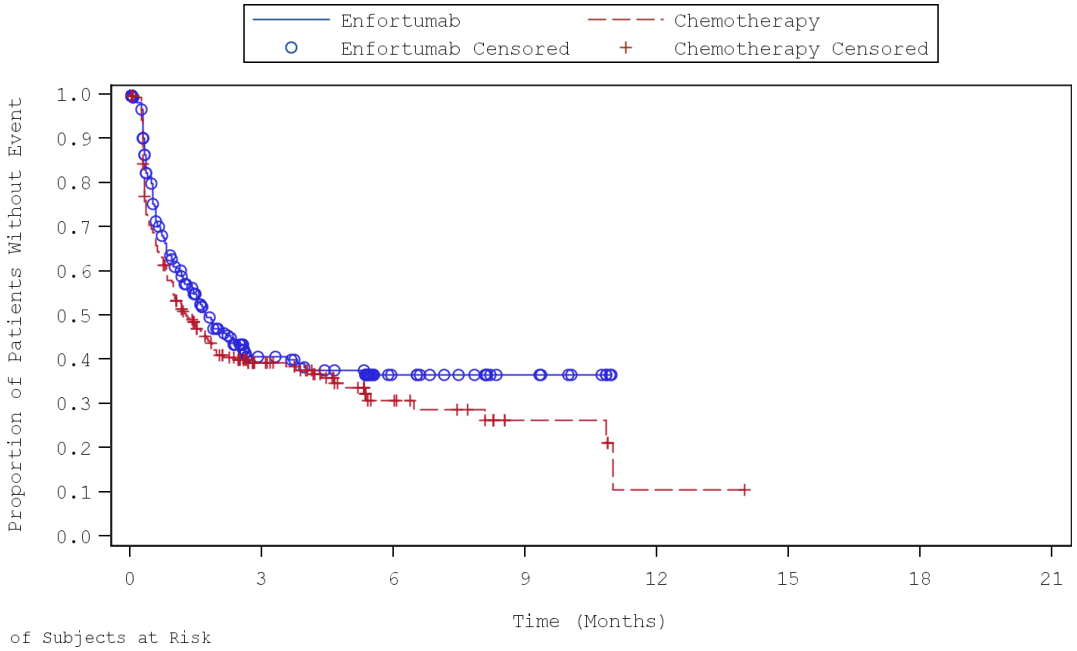
No. of Subjects at Risk

Enfortumab:	301	55	23	7	2	1	0	0
Chemotherapy:	307	43	15	3	1	0	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.813 (0.643, 1.028)
P-value: 0.08591
Enfortumab Median (95% CI): 1.51 (1.02, 1.97)
Chemotherapy Median (95% CI): 1.22 (0.99, 1.71)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_EORTC15_KM_FAS

Astellas: 7465-CL-0301
Figure EORTC15.NV.KM.FAS: EORTC Nausea and Vomiting Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Overall, Level: NA



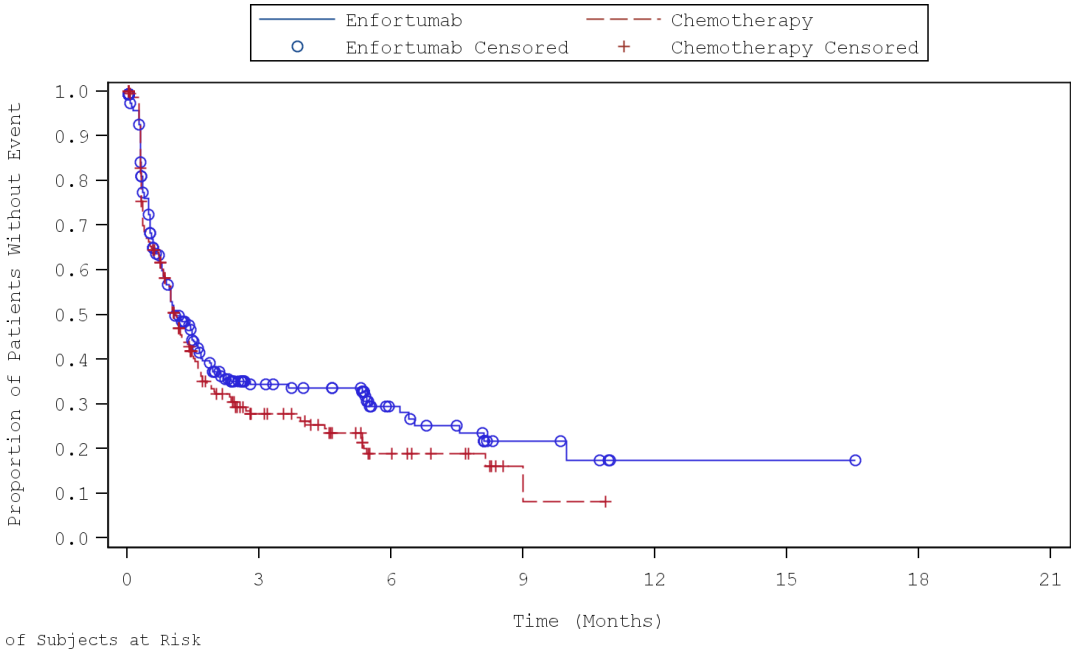
No. of Subjects at Risk

Enfortumab:	301	53	22	9	0	0	0	0
Chemotherapy:	307	53	18	5	1	0	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.825 (0.651, 1.045)
P-value: 0.12095
Enfortumab Median (95% CI): 1.71 (1.41, 2.37)
Chemotherapy Median (95% CI): 1.28 (0.99, 1.87)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_EORTC15_KM_FAS

Astellas: 7465-CL-0301
Figure EORTC15.PS.KM.FAS: EORTC Pain Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Overall, Level: NA



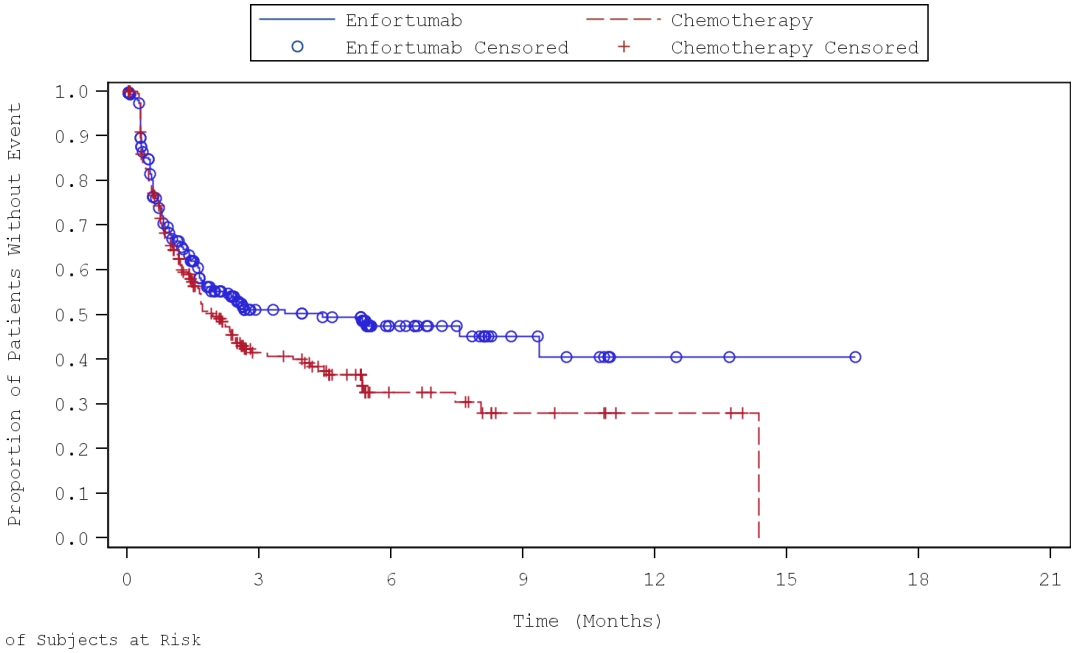
No. of Subjects at Risk

Enfortumab:	301	48	21	6	1	1	0	0
Chemotherapy:	307	38	13	2	0	0	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.868 (0.694, 1.085)
P-value: 0.21987
Enfortumab Median (95% CI): 1.08 (0.95, 1.54)
Chemotherapy Median (95% CI): 1.08 (0.95, 1.38)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_EORTC15_KM_FAS

Astellas: 7465-CL-0301
Figure EORTC15.DS.KM.FAS: EORTC Dyspnoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Overall, Level: NA



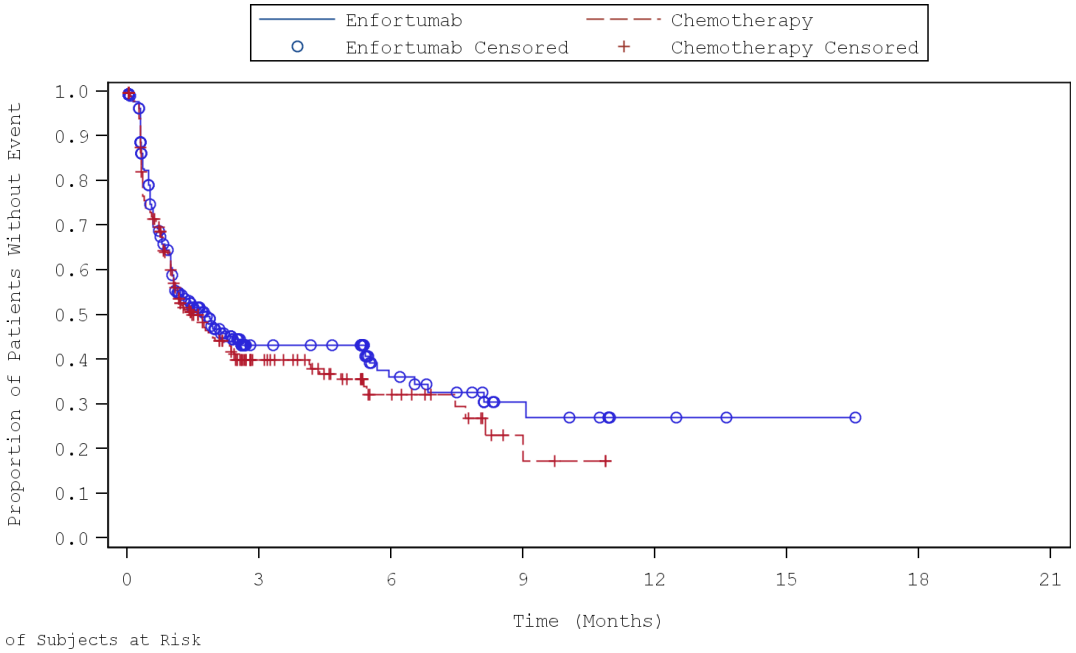
No. of Subjects at Risk

Enfortumab:	301	67	30	11	3	1	0	0
Chemotherapy:	307	54	17	7	3	0	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.784 (0.609, 1.009)
P-value: 0.05528
Enfortumab Median (95% CI): 4.44 (1.71, NC)
Chemotherapy Median (95% CI): 1.94 (1.51, 2.60)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_EORTC15_KM_FAS

Astellas: 7465-CL-0301
Figure EORTC15.SL.KM.FAS: EORTC Insomnia Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

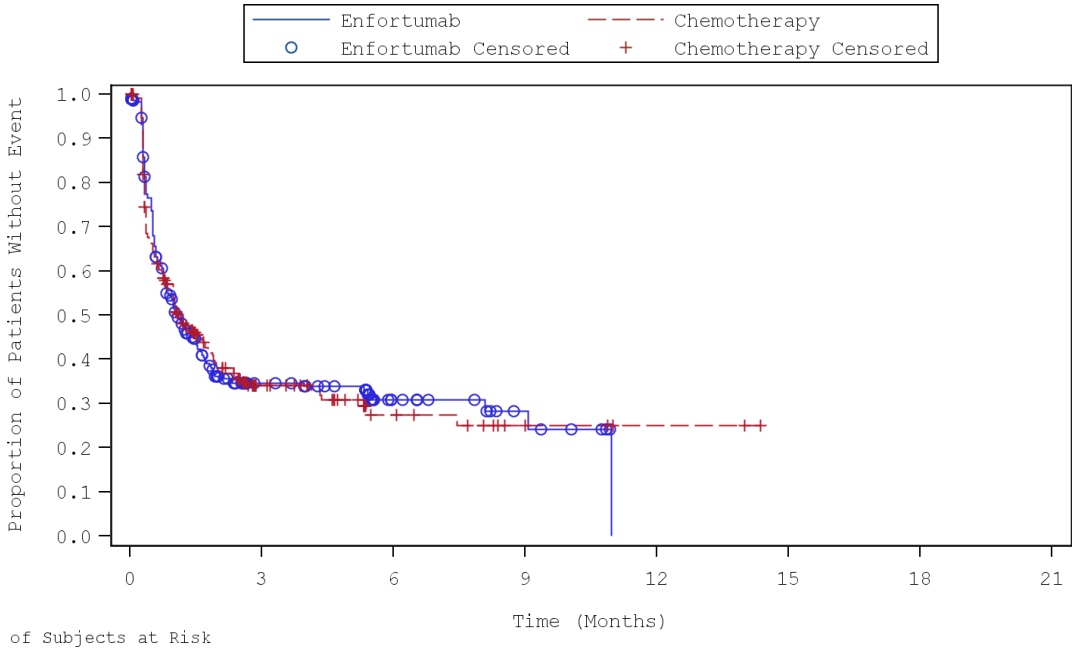
Enfortumab:	301	47	23	9	3	1	0	0
Chemotherapy:	307	47	17	4	0	0	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.850 (0.665, 1.086)
P-value: 0.19383

Enfortumab Median (95% CI): 1.81 (1.05, 2.60)
Chemotherapy Median (95% CI): 1.48 (1.08, 2.33)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_EORTC15_KM_FAS

Astellas: 7465-CL-0301
Figure EORTC15.AP.KM.FAS: EORTC Appetite Loss Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

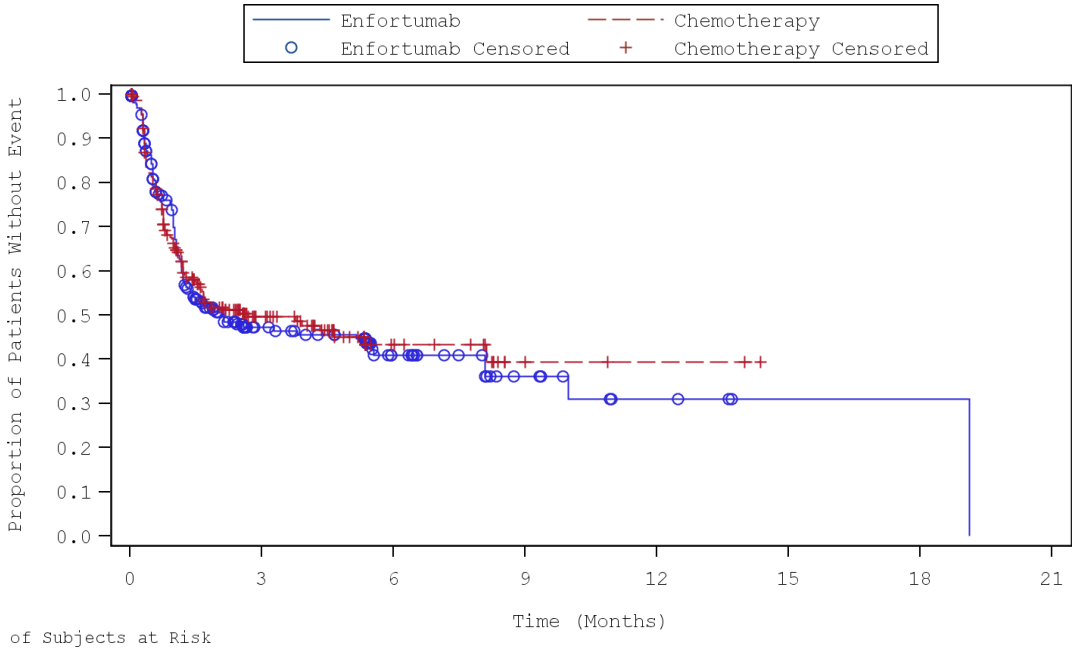
Enfortumab:	301	48	18	7	0	0	0
Chemotherapy:	307	38	13	5	2	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 1.002 (0.798, 1.258)
P-value: 0.96872

Enfortumab Median (95% CI): 1.08 (0.82, 1.51)
Chemotherapy Median (95% CI): 1.15 (0.99, 1.71)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_EORTC15_KM_FAS

Astellas: 7465-CL-0301
Figure EORTC15.CO.KM.FAS: EORTC Constipation Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Overall, Level: NA



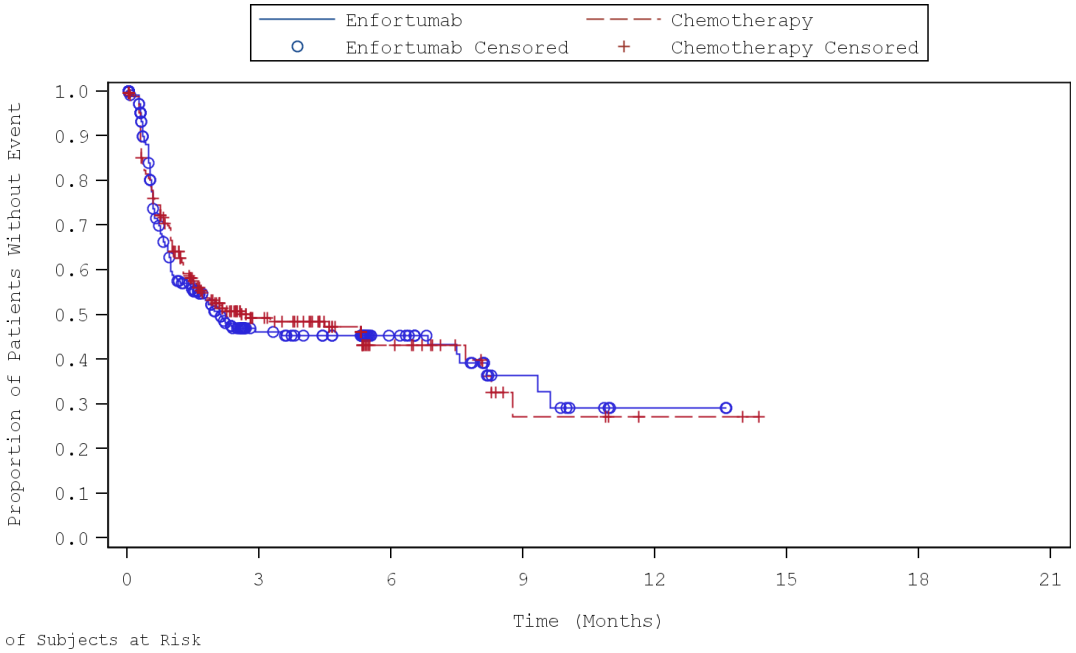
No. of Subjects at Risk

Enfortumab:	301	60	26	10	4	1	1	0
Chemotherapy:	307	57	17	4	2	0	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 1.073 (0.830, 1.389)
P-value: 0.58926
Enfortumab Median (95% CI): 2.14 (1.28, 5.52)
Chemotherapy Median (95% CI): 2.69 (1.51, 8.11)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_EORTC15_KM_FAS

Astellas: 7465-CL-0301
Figure EORTC15.DI.KM.FAS: EORTC Diarrhoea Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Overall, Level: NA



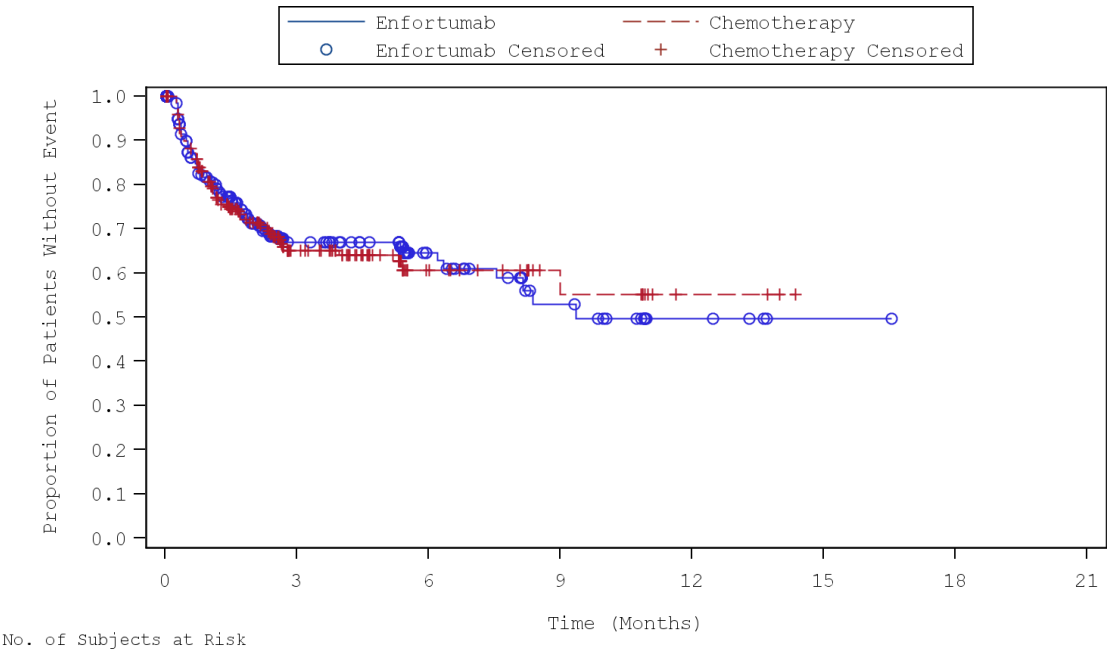
No. of Subjects at Risk

Enfortumab:	301	58	29	10	2	0	0	0
Chemotherapy:	307	60	21	5	2	0	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 1.005 (0.778, 1.298)
P-value: 0.93814
Enfortumab Median (95% CI): 2.14 (1.45, 7.49)
Chemotherapy Median (95% CI): 2.79 (1.58, 7.69)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_EORTC15_KM_FAS

Astellas: 7465-CL-0301
Figure EORTC15.FI.KM.FAS: EORTC Financial Difficulties Symptom Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

Enfortumab:	301	82	36	17	5	1	0	0
Chemotherapy:	307	74	24	11	3	0	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.926 (0.671, 1.279)
P-value: 0.63654
Enfortumab Median (95% CI): 9.36 (7.56, NC)
Chemotherapy Median (95% CI): NC (9.00, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_EORTC15_KM_FAS

2.6 Subgruppenanalysen zum Gesundheitszustand gemäß EQ-5D VAS

2.6.1 Primäranalyse (MID ≥ 7 mm)

Astellas: 7465-CL-0301
Table EQ5D7.VAS.KM.S1.FAS: EQ-5D VAS Score: Time to Deterioration of at least 7 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	65 (60.2)	59 (53.2)
	Median Survival Est. (95% CI)	1.18 (0.72, 1.91)	1.05 (0.76, 1.71)
	Hazard Ratio (95% CI)		0.975 (0.685, 1.387)
	Treatment P-value [a]		0.82154
	Interaction P-value [b]		0.44773
6 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.22 (0.12, 0.33)	4, 0.17 (0.09, 0.29)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.09 (0.02, 0.22)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D7.VAS.KM.S1.FAS: EQ-5D VAS Score: Time to Deterioration of at least 7 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	119 (61.7)	117 (59.7)
	Median Survival Est. (95% CI)	0.99 (0.76, 1.22)	0.95 (0.72, 1.08)
	Hazard Ratio (95% CI)		0.823 (0.637, 1.064)
	Treatment P-value [a]		0.14698
	Interaction P-value [b]		0.44773
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.18 (0.11, 0.25)	5, 0.11 (0.06, 0.19)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.16 (0.09, 0.24)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D7.VAS.KM.S2.FAS: EQ-5D VAS Score: Time to Deterioration of at least 7 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	149 (59.8)	127 (53.1)
	Median Survival Est. (95% CI)	1.02 (0.82, 1.45)	0.99 (0.76, 1.25)
	Hazard Ratio (95% CI)		0.869 (0.685, 1.102)
	Treatment P-value [a]		0.23008
	Interaction P-value [b]		0.54586
6 Months	Patients at Risk, Survival Est. (95% CI)	15, 0.21 (0.14, 0.28)	7, 0.18 (0.12, 0.25)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.12 (0.06, 0.21)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D7.VAS.KM.S2.FAS: EQ-5D VAS Score: Time to Deterioration of at least 7 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	35 (67.3)	49 (72.1)
	Median Survival Est. (95% CI)	0.79 (0.53, 1.05)	0.99 (0.76, 1.22)
	Hazard Ratio (95% CI)		1.012 (0.656, 1.562)
	Treatment P-value [a]		0.92143
	Interaction P-value [b]		0.54586
6 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.10 (0.03, 0.24)	2, 0.05 (0.01, 0.14)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.10 (0.03, 0.24)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D7.VAS.KM.S3.FAS: EQ-5D VAS Score: Time to Deterioration of at least 7 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	144 (60.5)	132 (56.9)
	Median Survival Est. (95% CI)	1.02 (0.79, 1.25)	0.99 (0.72, 1.18)
	Hazard Ratio (95% CI)		0.855 (0.675, 1.083)
	Treatment P-value [a]		0.18467
	Interaction P-value [b]		0.67939
6 Months	Patients at Risk, Survival Est. (95% CI)	15, 0.19 (0.13, 0.27)	7, 0.14 (0.08, 0.21)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.14 (0.07, 0.22)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D7.VAS.KM.S3.FAS: EQ-5D VAS Score: Time to Deterioration of at least 7 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	40 (63.5)	44 (58.7)
	Median Survival Est. (95% CI)	1.02 (0.59, 1.48)	0.99 (0.79, 1.28)
	Hazard Ratio (95% CI)		0.948 (0.617, 1.455)
	Treatment P-value [a]		0.76920
	Interaction P-value [b]		0.67939
6 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.18 (0.08, 0.31)	2, 0.16 (0.07, 0.27)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D7.VAS.KM.S4.FAS: EQ-5D VAS Score: Time to Deterioration of at least 7 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	66 (52.4)	58 (45.0)
	Median Survival Est. (95% CI)	1.18 (0.79, 1.94)	0.82 (0.56, 1.28)
	Hazard Ratio (95% CI)		0.760 (0.533, 1.082)
	Treatment P-value [a]		0.17483
	Interaction P-value [b]		0.37305
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.23 (0.14, 0.34)	5, 0.18 (0.09, 0.28)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.15 (0.06, 0.28)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D7.VAS.KM.S4.FAS: EQ-5D VAS Score: Time to Deterioration of at least 7 points (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	17 (39.5)	22 (50.0)
	Median Survival Est. (95% CI)	1.38 (0.59, NC)	1.02 (0.69, 2.46)
	Hazard Ratio (95% CI)		0.712 (0.377, 1.344)
	Treatment P-value [a]		0.43451
	Interaction P-value [b]		0.37305
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.36 (0.17, 0.56)	1, 0.16 (0.04, 0.36)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.36 (0.17, 0.56)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D7.VAS.KM.S4.FAS: EQ-5D VAS Score: Time to Deterioration of at least 7 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	101 (76.5)	96 (71.6)
	Median Survival Est. (95% CI)	0.99 (0.59, 1.22)	1.02 (0.76, 1.25)
	Hazard Ratio (95% CI)		1.006 (0.761, 1.331)
	Treatment P-value [a]		0.94527
	Interaction P-value [b]		0.37305
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.12 (0.06, 0.20)	3, 0.11 (0.05, 0.19)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D7.VAS.KM.S5.FAS: EQ-5D VAS Score: Time to Deterioration of at least 7 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	85 (70.8)	75 (60.5)
	Median Survival Est. (95% CI)	1.02 (0.62, 1.41)	1.02 (0.76, 1.28)
	Hazard Ratio (95% CI)		1.035 (0.758, 1.412)
	Treatment P-value [a]		0.92758
	Interaction P-value [b]		0.15464
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.15 (0.08, 0.24)	3, 0.20 (0.12, 0.30)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D7.VAS.KM.S5.FAS: EQ-5D VAS Score: Time to Deterioration of at least 7 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	99 (54.7)	101 (55.2)
	Median Survival Est. (95% CI)	1.02 (0.76, 1.38)	0.95 (0.72, 1.18)
	Hazard Ratio (95% CI)		0.764 (0.579, 1.009)
	Treatment P-value [a]		0.06077
	Interaction P-value [b]		0.15464
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.22 (0.14, 0.32)	6, 0.10 (0.05, 0.17)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.19 (0.11, 0.29)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D7.VAS.KM.S6.FAS: EQ-5D VAS Score: Time to Deterioration of at least 7 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	53 (57.0)	46 (48.4)
	Median Survival Est. (95% CI)	0.76 (0.56, 1.38)	0.99 (0.56, 1.28)
	Hazard Ratio (95% CI)		0.877 (0.590, 1.304)
	Treatment P-value [a]		0.58324
	Interaction P-value [b]		0.97850
6 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.22 (0.12, 0.34)	1, 0.17 (0.08, 0.29)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.12 (0.03, 0.27)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D7.VAS.KM.S6.FAS: EQ-5D VAS Score: Time to Deterioration of at least 7 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	131 (63.0)	130 (61.3)
	Median Survival Est. (95% CI)	1.02 (0.85, 1.41)	0.99 (0.76, 1.18)
	Hazard Ratio (95% CI)		0.872 (0.684, 1.111)
	Treatment P-value [a]		0.25391
	Interaction P-value [b]		0.97850
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.18 (0.11, 0.25)	8, 0.13 (0.07, 0.20)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.13 (0.06, 0.22)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D7.VAS.KM.S7.FAS: EQ-5D VAS Score: Time to Deterioration of at least 7 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	91 (64.5)	64 (57.1)
	Median Survival Est. (95% CI)	1.02 (0.62, 1.28)	1.02 (0.76, 1.51)
	Hazard Ratio (95% CI)		0.974 (0.707, 1.341)
	Treatment P-value [a]		0.87479
	Interaction P-value [b]		0.61713
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.13 (0.06, 0.24)	2, 0.16 (0.08, 0.27)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D7.VAS.KM.S7.FAS: EQ-5D VAS Score: Time to Deterioration of at least 7 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	49 (56.3)	69 (59.0)
	Median Survival Est. (95% CI)	0.82 (0.59, 1.38)	0.99 (0.72, 1.08)
	Hazard Ratio (95% CI)		0.879 (0.609, 1.269)
	Treatment P-value [a]		0.48263
	Interaction P-value [b]		0.61713
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.20 (0.10, 0.32)	3, 0.11 (0.05, 0.22)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.16 (0.07, 0.29)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D7.VAS.KM.S7.FAS: EQ-5D VAS Score: Time to Deterioration of at least 7 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	44 (60.3)	43 (55.1)
	Median Survival Est. (95% CI)	1.03 (0.72, 2.00)	0.99 (0.53, 1.61)
	Hazard Ratio (95% CI)		0.747 (0.490, 1.139)
	Treatment P-value [a]		0.19880
	Interaction P-value [b]		0.61713
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.26 (0.15, 0.39)	4, 0.13 (0.05, 0.25)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.15 (0.04, 0.32)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EQ5D7.VAS.KM.S8.FAS: EQ-5D VAS Score: Time to Deterioration of at least 7 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	60 (61.2)	71 (66.4)
	Median Survival Est. (95% CI)	0.95 (0.59, 1.22)	0.82 (0.56, 1.05)
	Hazard Ratio (95% CI)		0.854 (0.605, 1.204)
	Treatment P-value [a]		0.36261
	Interaction P-value [b]		0.81154
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.23 (0.14, 0.33)	5, 0.15 (0.08, 0.25)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Astellas: 7465-CL-0301
Table EQ5D7.VAS.KM.S8.FAS: EQ-5D VAS Score: Time to Deterioration of at least 7 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	124 (61.1)	105 (52.5)
	Median Survival Est. (95% CI)	1.02 (0.79, 1.51)	1.02 (0.82, 1.45)
	Hazard Ratio (95% CI)		0.900 (0.693, 1.168)
	Treatment P-value [a]		0.40278
	Interaction P-value [b]		0.81154
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.17 (0.10, 0.25)	4, 0.12 (0.06, 0.20)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.15 (0.09, 0.23)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D7.VAS.KM.S9.FAS: EQ-5D VAS Score: Time to Deterioration of at least 7 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	161 (61.5)	151 (55.9)
	Median Survival Est. (95% CI)	1.02 (0.79, 1.25)	0.99 (0.76, 1.12)
	Hazard Ratio (95% CI)		0.862 (0.690, 1.077)
	Treatment P-value [a]		0.18778
	Interaction P-value [b]		0.74320
6 Months	Patients at Risk, Survival Est. (95% CI)	16, 0.19 (0.13, 0.26)	8, 0.14 (0.09, 0.21)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.13 (0.07, 0.21)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EQ5D7.VAS.KM.S9.FAS: EQ-5D VAS Score: Time to Deterioration of at least 7 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	23 (59.0)	25 (67.6)
	Median Survival Est. (95% CI)	1.02 (0.53, 2.63)	1.05 (0.39, 2.33)
	Hazard Ratio (95% CI)		0.954 (0.541, 1.682)
	Treatment P-value [a]		0.81592
	Interaction P-value [b]		0.74320
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.14 (0.01, 0.40)	1, 0.09 (0.01, 0.30)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D7.VAS.KM.S10.FAS: EQ-5D VAS Score: Time to Deterioration of at least 7 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	43 (70.5)	31 (62.0)
	Median Survival Est. (95% CI)	1.02 (0.59, 1.22)	0.99 (0.53, 1.91)
	Hazard Ratio (95% CI)		1.079 (0.679, 1.714)
	Treatment P-value [a]		0.66427
	Interaction P-value [b]		0.31772
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.14 (0.06, 0.26)	3, 0.14 (0.05, 0.30)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EQ5D7.VAS.KM.S10.FAS: EQ-5D VAS Score: Time to Deterioration of at least 7 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	120 (58.0)	124 (57.7)
	Median Survival Est. (95% CI)	0.99 (0.72, 1.45)	0.99 (0.72, 1.18)
	Hazard Ratio (95% CI)		0.824 (0.640, 1.061)
	Treatment P-value [a]		0.12923
	Interaction P-value [b]		0.31772
6 Months	Patients at Risk, Survival Est. (95% CI)	14, 0.22 (0.15, 0.30)	6, 0.13 (0.07, 0.20)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.14 (0.06, 0.24)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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2.6.2 Primäranalyse (MID ≥ 10 mm)

Astellas: 7465-CL-0301
Table EQ5D10.VAS.KM.S1.FAS: EQ-5D VAS Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	56 (51.9)	56 (50.5)
	Median Survival Est. (95% CI)	1.58 (0.95, 2.17)	1.71 (0.99, 2.27)
	Hazard Ratio (95% CI)		0.889 (0.614, 1.288)
	Treatment P-value [a]		0.53937
	Interaction P-value [b]		0.57581
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.28 (0.16, 0.40)	6, 0.23 (0.13, 0.35)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.23 (0.12, 0.37)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EQ5D10.VAS.KM.S1.FAS: EQ-5D VAS Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	108 (56.0)	112 (57.1)
	Median Survival Est. (95% CI)	1.02 (0.89, 1.51)	1.02 (0.95, 1.38)
	Hazard Ratio (95% CI)		0.781 (0.599, 1.018)
	Treatment P-value [a]		0.06824
	Interaction P-value [b]		0.57581
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.24 (0.16, 0.33)	5, 0.12 (0.06, 0.20)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.19 (0.11, 0.29)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EQ5D10.VAS.KM.S2.FAS: EQ-5D VAS Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	133 (53.4)	120 (50.2)
	Median Survival Est. (95% CI)	1.45 (1.02, 1.94)	1.25 (0.99, 1.77)
	Hazard Ratio (95% CI)		0.827 (0.646, 1.059)
	Treatment P-value [a]		0.12908
	Interaction P-value [b]		0.71864
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.27 (0.20, 0.35)	9, 0.21 (0.14, 0.30)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.21 (0.14, 0.30)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EQ5D10.VAS.KM.S2.FAS: EQ-5D VAS Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	31 (59.6)	48 (70.6)
	Median Survival Est. (95% CI)	0.89 (0.53, 1.25)	1.08 (0.82, 1.28)
	Hazard Ratio (95% CI)		0.909 (0.579, 1.429)
	Treatment P-value [a]		0.72011
	Interaction P-value [b]		0.71864
6 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.17 (0.05, 0.35)	2, 0.05 (0.01, 0.14)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.17 (0.05, 0.35)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EQ5D10.VAS.KM.S3.FAS: EQ-5D VAS Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	130 (54.6)	127 (54.7)
	Median Survival Est. (95% CI)	1.22 (0.95, 1.64)	1.18 (0.95, 1.71)
	Hazard Ratio (95% CI)		0.807 (0.632, 1.031)
	Treatment P-value [a]		0.07791
	Interaction P-value [b]		0.83623
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.25 (0.18, 0.34)	8, 0.16 (0.09, 0.23)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.20 (0.13, 0.29)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Astellas: 7465-CL-0301
Table EQ5D10.VAS.KM.S3.FAS: EQ-5D VAS Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	34 (54.0)	41 (54.7)
	Median Survival Est. (95% CI)	1.48 (0.72, 2.30)	1.08 (0.82, 1.74)
	Hazard Ratio (95% CI)		0.852 (0.541, 1.344)
	Treatment P-value [a]		0.50969
	Interaction P-value [b]		0.83623
6 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.25 (0.11, 0.41)	3, 0.20 (0.10, 0.32)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EQ5D10.VAS.KM.S4.FAS: EQ-5D VAS Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	62 (49.2)	58 (45.0)
	Median Survival Est. (95% CI)	1.22 (0.82, 2.00)	0.85 (0.69, 1.28)
	Hazard Ratio (95% CI)		0.723 (0.505, 1.034)
	Treatment P-value [a]		0.11237
	Interaction P-value [b]		0.67816
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.25 (0.14, 0.37)	5, 0.17 (0.09, 0.28)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.21 (0.11, 0.34)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EQ5D10.VAS.KM.S4.FAS: EQ-5D VAS Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	16 (37.2)	16 (36.4)
	Median Survival Est. (95% CI)	1.68 (0.62, NC)	2.46 (0.99, NC)
	Hazard Ratio (95% CI)		0.987 (0.493, 1.975)
	Treatment P-value [a]		0.92553
	Interaction P-value [b]		0.67816
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.36 (0.16, 0.56)	2, 0.41 (0.23, 0.59)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.36 (0.16, 0.56)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Table EQ5D10.VAS.KM.S4.FAS: EQ-5D VAS Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	86 (65.2)	94 (70.1)
	Median Survival Est. (95% CI)	1.18 (0.89, 1.54)	1.25 (0.99, 1.71)
	Hazard Ratio (95% CI)		0.844 (0.630, 1.131)
	Treatment P-value [a]		0.22468
	Interaction P-value [b]		0.67816
6 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.24 (0.16, 0.34)	4, 0.11 (0.05, 0.20)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Table EQ5D10.VAS.KM.S5.FAS: EQ-5D VAS Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	72 (60.0)	71 (57.3)
	Median Survival Est. (95% CI)	1.41 (0.95, 1.81)	1.25 (0.99, 1.91)
	Hazard Ratio (95% CI)		0.911 (0.656, 1.266)
	Treatment P-value [a]		0.54614
	Interaction P-value [b]		0.38354
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.24 (0.15, 0.35)	4, 0.25 (0.16, 0.35)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EQ5D10.VAS.KM.S5.FAS: EQ-5D VAS Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	92 (50.8)	97 (53.0)
	Median Survival Est. (95% CI)	1.18 (0.92, 1.94)	1.02 (0.82, 1.71)
	Hazard Ratio (95% CI)		0.751 (0.565, 0.999)
	Treatment P-value [a]		0.04782
	Interaction P-value [b]		0.38354
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.26 (0.17, 0.36)	7, 0.11 (0.05, 0.19)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.22 (0.13, 0.34)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EQ5D10.VAS.KM.S6.FAS: EQ-5D VAS Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	47 (50.5)	45 (47.4)
	Median Survival Est. (95% CI)	1.02 (0.59, 2.23)	1.02 (0.82, 1.68)
	Hazard Ratio (95% CI)		0.797 (0.529, 1.202)
	Treatment P-value [a]		0.35637
	Interaction P-value [b]		0.88911
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.27 (0.15, 0.41)	1, 0.16 (0.07, 0.28)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.23 (0.11, 0.37)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EQ5D10.VAS.KM.S6.FAS: EQ-5D VAS Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	117 (56.3)	123 (58.0)
	Median Survival Est. (95% CI)	1.45 (1.02, 1.81)	1.18 (0.99, 1.81)
	Hazard Ratio (95% CI)		0.825 (0.640, 1.063)
	Treatment P-value [a]		0.12550
	Interaction P-value [b]		0.88911
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.24 (0.16, 0.33)	10, 0.16 (0.10, 0.24)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.20 (0.12, 0.29)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EQ5D10.VAS.KM.S7.FAS: EQ-5D VAS Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	79 (56.0)	62 (55.4)
	Median Survival Est. (95% CI)	1.22 (0.95, 1.94)	1.28 (0.82, 1.91)
	Hazard Ratio (95% CI)		0.878 (0.630, 1.225)
	Treatment P-value [a]		0.44916
	Interaction P-value [b]		0.75065
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.22 (0.12, 0.35)	3, 0.15 (0.06, 0.28)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EQ5D10.VAS.KM.S7.FAS: EQ-5D VAS Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	44 (50.6)	63 (53.8)
	Median Survival Est. (95% CI)	1.45 (0.82, 2.07)	1.18 (0.95, 2.14)
	Hazard Ratio (95% CI)		0.823 (0.560, 1.210)
	Treatment P-value [a]		0.29758
	Interaction P-value [b]		0.75065
6 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.25 (0.14, 0.39)	4, 0.18 (0.09, 0.30)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.21 (0.10, 0.35)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EQ5D10.VAS.KM.S7.FAS: EQ-5D VAS Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	41 (56.2)	43 (55.1)
	Median Survival Est. (95% CI)	1.12 (0.72, 2.14)	1.05 (0.56, 1.71)
	Hazard Ratio (95% CI)		0.713 (0.464, 1.094)
	Treatment P-value [a]		0.15382
	Interaction P-value [b]		0.75065
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.28 (0.16, 0.42)	4, 0.12 (0.04, 0.25)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.24 (0.11, 0.38)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EQ5D10.VAS.KM.S8.FAS: EQ-5D VAS Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	54 (55.1)	68 (63.6)
	Median Survival Est. (95% CI)	1.02 (0.72, 1.45)	0.99 (0.82, 1.28)
	Hazard Ratio (95% CI)		0.809 (0.566, 1.157)
	Treatment P-value [a]		0.28914
	Interaction P-value [b]		0.87519
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.28 (0.18, 0.39)	5, 0.17 (0.09, 0.27)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EQ5D10.VAS.KM.S8.FAS: EQ-5D VAS Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	110 (54.2)	100 (50.0)
	Median Survival Est. (95% CI)	1.51 (0.99, 2.10)	1.45 (0.99, 1.91)
	Hazard Ratio (95% CI)		0.839 (0.639, 1.100)
	Treatment P-value [a]		0.17261
	Interaction P-value [b]		0.87519
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.24 (0.15, 0.33)	6, 0.15 (0.08, 0.24)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.19 (0.11, 0.29)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EQ5D10.VAS.KM.S9.FAS: EQ-5D VAS Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	145 (55.3)	145 (53.7)
	Median Survival Est. (95% CI)	1.22 (0.95, 1.68)	1.18 (0.99, 1.61)
	Hazard Ratio (95% CI)		0.820 (0.651, 1.033)
	Treatment P-value [a]		0.09174
	Interaction P-value [b]		0.95160
6 Months	Patients at Risk, Survival Est. (95% CI)	18, 0.25 (0.18, 0.32)	10, 0.16 (0.10, 0.23)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.22 (0.15, 0.29)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EQ5D10.VAS.KM.S9.FAS: EQ-5D VAS Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	19 (48.7)	23 (62.2)
	Median Survival Est. (95% CI)	1.45 (0.99, NC)	1.25 (0.72, 2.69)
	Hazard Ratio (95% CI)		0.804 (0.437, 1.476)
	Treatment P-value [a]		0.43012
	Interaction P-value [b]		0.95160
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.22 (0.02, 0.56)	1, 0.12 (0.01, 0.37)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EQ5D10.VAS.KM.S10.FAS: EQ-5D VAS Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	38 (62.3)	31 (62.0)
	Median Survival Est. (95% CI)	1.18 (0.79, 1.64)	1.25 (0.95, 1.94)
	Hazard Ratio (95% CI)		0.924 (0.575, 1.486)
	Treatment P-value [a]		0.84317
	Interaction P-value [b]		0.57131
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.20 (0.08, 0.36)	4, 0.18 (0.07, 0.34)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D10.VAS.KM.S10.FAS: EQ-5D VAS Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	109 (52.7)	117 (54.4)
	Median Survival Est. (95% CI)	1.28 (0.89, 1.71)	1.18 (0.95, 1.68)
	Hazard Ratio (95% CI)		0.790 (0.608, 1.027)
	Treatment P-value [a]		0.07614
	Interaction P-value [b]		0.57131
6 Months	Patients at Risk, Survival Est. (95% CI)	16, 0.27 (0.19, 0.36)	6, 0.14 (0.08, 0.23)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.23 (0.15, 0.33)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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2.6.3 Sensitivitätsanalyse (Responderschwelle ≥ 15 Punkte)

Astellas: 7465-CL-0301
Table EQ5D15.VAS.KM.S1.FAS: EQ-5D VAS Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	45 (41.7)	46 (41.4)
	Median Survival Est. (95% CI)	5.19 (1.54, 8.38)	2.46 (1.48, 5.59)
	Hazard Ratio (95% CI)		0.829 (0.550, 1.251)
	Treatment P-value [a]		0.36346
	Interaction P-value [b]		0.87136
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.45 (0.32, 0.57)	7, 0.37 (0.24, 0.50)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.29 (0.13, 0.46)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D15.VAS.KM.S1.FAS: EQ-5D VAS Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	87 (45.1)	90 (45.9)
	Median Survival Est. (95% CI)	2.23 (1.41, 5.49)	1.71 (1.25, 2.37)
	Hazard Ratio (95% CI)		0.795 (0.592, 1.069)
	Treatment P-value [a]		0.14343
	Interaction P-value [b]		0.87136
6 Months	Patients at Risk, Survival Est. (95% CI)	18, 0.37 (0.27, 0.46)	9, 0.28 (0.19, 0.38)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.20 (0.06, 0.40)	1, 0.20 (0.10, 0.33)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D15.VAS.KM.S2.FAS: EQ-5D VAS Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	107 (43.0)	96 (40.2)
	Median Survival Est. (95% CI)	2.83 (1.68, 6.54)	2.14 (1.61, 3.75)
	Hazard Ratio (95% CI)		0.833 (0.632, 1.099)
	Treatment P-value [a]		0.18818
	Interaction P-value [b]		0.94798
6 Months	Patients at Risk, Survival Est. (95% CI)	26, 0.42 (0.33, 0.50)	12, 0.36 (0.27, 0.45)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.25 (0.11, 0.41)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D15.VAS.KM.S2.FAS: EQ-5D VAS Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	25 (48.1)	40 (58.8)
	Median Survival Est. (95% CI)	1.74 (0.79, 5.88)	1.18 (0.99, 2.56)
	Hazard Ratio (95% CI)		0.818 (0.496, 1.348)
	Treatment P-value [a]		0.44131
	Interaction P-value [b]		0.94798
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.30 (0.13, 0.49)	4, 0.18 (0.07, 0.31)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.20 (0.05, 0.43)	1, 0.13 (0.04, 0.27)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EQ5D15.VAS.KM.S3.FAS: EQ-5D VAS Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	107 (45.0)	107 (46.1)
	Median Survival Est. (95% CI)	2.14 (1.58, 5.68)	1.74 (1.38, 2.37)
	Hazard Ratio (95% CI)		0.770 (0.589, 1.008)
	Treatment P-value [a]		0.04701
	Interaction P-value [b]		0.58923
6 Months	Patients at Risk, Survival Est. (95% CI)	24, 0.39 (0.30, 0.48)	11, 0.29 (0.20, 0.38)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.21 (0.09, 0.35)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EQ5D15.VAS.KM.S3.FAS: EQ-5D VAS Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	25 (39.7)	29 (38.7)
	Median Survival Est. (95% CI)	5.36 (1.02, NC)	2.46 (1.15, NC)
	Hazard Ratio (95% CI)		0.908 (0.532, 1.552)
	Treatment P-value [a]		0.77236
	Interaction P-value [b]		0.58923
6 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.43 (0.26, 0.59)	5, 0.37 (0.22, 0.52)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.37 (0.22, 0.52)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EQ5D15.VAS.KM.S4.FAS: EQ-5D VAS Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	49 (38.9)	48 (37.2)
	Median Survival Est. (95% CI)	5.36 (1.68, 6.83)	1.48 (0.99, 2.00)
	Hazard Ratio (95% CI)		0.710 (0.477, 1.058)
	Treatment P-value [a]		0.12322
	Interaction P-value [b]		0.51435
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.37 (0.23, 0.50)	7, 0.33 (0.22, 0.45)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.32 (0.17, 0.47)	1, 0.26 (0.13, 0.42)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EQ5D15.VAS.KM.S4.FAS: EQ-5D VAS Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	14 (32.6)	12 (27.3)
	Median Survival Est. (95% CI)	5.45 (1.58, NC)	2.69 (2.23, NC)
	Hazard Ratio (95% CI)		1.183 (0.546, 2.559)
	Treatment P-value [a]		0.59207
	Interaction P-value [b]		0.51435
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.39 (0.17, 0.61)	2, 0.50 (0.28, 0.68)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.39 (0.17, 0.61)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EQ5D15.VAS.KM.S4.FAS: EQ-5D VAS Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	69 (52.3)	76 (56.7)
	Median Survival Est. (95% CI)	1.97 (1.22, 6.54)	2.14 (1.38, 2.79)
	Hazard Ratio (95% CI)		0.806 (0.581, 1.117)
	Treatment P-value [a]		0.13590
	Interaction P-value [b]		0.51435
6 Months	Patients at Risk, Survival Est. (95% CI)	16, 0.42 (0.32, 0.52)	7, 0.26 (0.17, 0.37)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EQ5D15.VAS.KM.S5.FAS: EQ-5D VAS Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	57 (47.5)	51 (41.1)
	Median Survival Est. (95% CI)	2.14 (1.41, 5.68)	3.06 (1.68, 7.69)
	Hazard Ratio (95% CI)		1.065 (0.729, 1.555)
	Treatment P-value [a]		0.82322
	Interaction P-value [b]		0.05135
6 Months	Patients at Risk, Survival Est. (95% CI)	14, 0.38 (0.26, 0.50)	8, 0.47 (0.36, 0.58)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.16 (0.03, 0.38)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EQ5D15.VAS.KM.S5.FAS: EQ-5D VAS Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	75 (41.4)	85 (46.4)
	Median Survival Est. (95% CI)	2.56 (1.68, 6.83)	1.61 (1.15, 2.10)
	Hazard Ratio (95% CI)		0.655 (0.480, 0.893)
	Treatment P-value [a]		0.00726
	Interaction P-value [b]		0.05135
6 Months	Patients at Risk, Survival Est. (95% CI)	16, 0.41 (0.31, 0.51)	8, 0.19 (0.11, 0.29)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.26 (0.14, 0.40)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EQ5D15.VAS.KM.S6.FAS: EQ-5D VAS Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	38 (40.9)	39 (41.1)
	Median Survival Est. (95% CI)	1.97 (0.99, NC)	1.61 (0.99, 2.23)
	Hazard Ratio (95% CI)		0.725 (0.463, 1.135)
	Treatment P-value [a]		0.21191
	Interaction P-value [b]		0.59248
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.41 (0.28, 0.54)	3, 0.28 (0.16, 0.42)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.36 (0.21, 0.51)	1, 0.19 (0.05, 0.38)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EQ5D15.VAS.KM.S6.FAS: EQ-5D VAS Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	94 (45.2)	97 (45.8)
	Median Survival Est. (95% CI)	2.83 (1.74, 5.88)	2.14 (1.51, 3.75)
	Hazard Ratio (95% CI)		0.838 (0.631, 1.113)
	Treatment P-value [a]		0.19465
	Interaction P-value [b]		0.59248
6 Months	Patients at Risk, Survival Est. (95% CI)	19, 0.39 (0.29, 0.48)	13, 0.32 (0.23, 0.41)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.20 (0.08, 0.36)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EQ5D15.VAS.KM.S7.FAS: EQ-5D VAS Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	60 (42.6)	50 (44.6)
	Median Survival Est. (95% CI)	5.36 (1.54, 9.36)	2.14 (1.18, 3.75)
	Hazard Ratio (95% CI)		0.776 (0.533, 1.130)
	Treatment P-value [a]		0.19397
	Interaction P-value [b]		0.91603
6 Months	Patients at Risk, Survival Est. (95% CI)	14, 0.45 (0.33, 0.56)	4, 0.30 (0.17, 0.44)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D15.VAS.KM.S7.FAS: EQ-5D VAS Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	37 (42.5)	51 (43.6)
	Median Survival Est. (95% CI)	2.07 (1.22, 5.49)	2.46 (1.25, 4.60)
	Hazard Ratio (95% CI)		0.873 (0.571, 1.334)
	Treatment P-value [a]		0.53685
	Interaction P-value [b]		0.91603
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.35 (0.22, 0.50)	6, 0.29 (0.17, 0.43)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.31 (0.17, 0.46)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D15.VAS.KM.S7.FAS: EQ-5D VAS Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	35 (47.9)	35 (44.9)
	Median Survival Est. (95% CI)	2.14 (0.92, 6.83)	1.61 (0.99, 2.14)
	Hazard Ratio (95% CI)		0.797 (0.498, 1.273)
	Treatment P-value [a]		0.37710
	Interaction P-value [b]		0.91603
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.36 (0.22, 0.51)	6, 0.31 (0.18, 0.45)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.30 (0.15, 0.47)	1, 0.23 (0.09, 0.41)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D15.VAS.KM.S8.FAS: EQ-5D VAS Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	47 (48.0)	56 (52.3)
	Median Survival Est. (95% CI)	1.45 (0.99, 2.56)	1.68 (1.02, 2.37)
	Hazard Ratio (95% CI)		0.883 (0.599, 1.302)
	Treatment P-value [a]		0.60480
	Interaction P-value [b]		0.64757
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.39 (0.27, 0.50)	5, 0.26 (0.15, 0.38)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D15.VAS.KM.S8.FAS: EQ-5D VAS Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	85 (41.9)	80 (40.0)
	Median Survival Est. (95% CI)	5.36 (1.94, 6.83)	2.14 (1.58, 3.91)
	Hazard Ratio (95% CI)		0.787 (0.579, 1.069)
	Treatment P-value [a]		0.10965
	Interaction P-value [b]		0.64757
6 Months	Patients at Risk, Survival Est. (95% CI)	20, 0.40 (0.30, 0.50)	11, 0.34 (0.24, 0.44)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.25 (0.12, 0.40)	1, 0.18 (0.08, 0.32)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D15.VAS.KM.S9.FAS: EQ-5D VAS Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	114 (43.5)	119 (44.1)
	Median Survival Est. (95% CI)	2.53 (1.74, 5.88)	1.81 (1.45, 2.37)
	Hazard Ratio (95% CI)		0.770 (0.595, 0.997)
	Treatment P-value [a]		0.04902
	Interaction P-value [b]		0.31732
6 Months	Patients at Risk, Survival Est. (95% CI)	29, 0.41 (0.33, 0.49)	13, 0.29 (0.21, 0.38)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.25 (0.13, 0.40)	1, 0.18 (0.09, 0.29)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D15.VAS.KM.S9.FAS: EQ-5D VAS Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	18 (46.2)	17 (45.9)
	Median Survival Est. (95% CI)	4.44 (1.02, NC)	2.69 (0.95, NC)
	Hazard Ratio (95% CI)		1.107 (0.570, 2.150)
	Treatment P-value [a]		0.83318
	Interaction P-value [b]		0.31732
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.21 (0.02, 0.55)	3, 0.37 (0.14, 0.61)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D15.VAS.KM.S10.FAS: EQ-5D VAS Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	31 (50.8)	27 (54.0)
	Median Survival Est. (95% CI)	1.94 (1.02, 7.16)	1.74 (0.99, 5.59)
	Hazard Ratio (95% CI)		0.771 (0.460, 1.292)
	Treatment P-value [a]		0.34365
	Interaction P-value [b]		0.81938
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.37 (0.22, 0.53)	5, 0.29 (0.14, 0.47)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D15.VAS.KM.S10.FAS: EQ-5D VAS Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	88 (42.5)	92 (42.8)
	Median Survival Est. (95% CI)	4.44 (1.58, 6.83)	2.14 (1.45, 2.79)
	Hazard Ratio (95% CI)		0.826 (0.616, 1.108)
	Treatment P-value [a]		0.20060
	Interaction P-value [b]		0.81938
6 Months	Patients at Risk, Survival Est. (95% CI)	23, 0.41 (0.32, 0.50)	10, 0.31 (0.22, 0.41)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.23 (0.10, 0.41)	1, 0.24 (0.14, 0.36)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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2.6.4 MMRM-Modell

Astellas: 7465-CL-0301
Table EQ5D.VAS.MM.S1.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EQ-5D VAS Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Age Group 1

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
<65 years	N, n	108, 82	111, 68	
	Baseline Mean (SD)	67.09 (18.07)	73.24 (19.73)	
	Change from Baseline LS Mean (SE)	-1.11 (1.22)	-2.02 (1.33)	0.91 (-2.63, 4.46)
	Treatment P-value			0.61223
	Hedge's g (95% CI)			0.07 (-0.25, 0.39)
>=65 years	N, n	193, 146	196, 124	
	Baseline Mean (SD)	68.90 (17.88)	69.27 (17.28)	
	Change from Baseline LS Mean (SE)	-3.48 (0.92)	-6.26 (1.01)	2.78 (0.10, 5.46)
	Treatment P-value			0.04184
	Hedge's g (95% CI)			0.19 (-0.05, 0.43)
	Interaction P-value [b]			0.17358

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients. Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D.VAS.MM.S2.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EQ-5D VAS Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Age Group 2

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
<75 years	N, n	249, 191	239, 146	
	Baseline Mean (SD)	67.87 (18.54)	70.62 (19.14)	
	Change from Baseline LS Mean (SE)	-2.21 (0.80)	-3.53 (0.92)	1.32 (-1.08, 3.72)
	Treatment P-value			0.27942
	Hedge's g (95% CI)			0.09 (-0.12, 0.31)
>=75 years	N, n	52, 37	68, 46	
	Baseline Mean (SD)	70.19 (14.39)	70.85 (15.17)	
	Change from Baseline LS Mean (SE)	-4.90 (1.86)	-8.69 (1.66)	3.79 (-1.12, 8.69)
	Treatment P-value			0.12975
	Hedge's g (95% CI)			0.27 (-0.16, 0.71)
	Interaction P-value [b]			0.24334

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D.VAS.MM.S3.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EQ-5D VAS Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Gender

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Male	N, n	238, 180	232, 147	
	Baseline Mean (SD)	68.71 (17.24)	70.79 (17.22)	
	Change from Baseline LS Mean (SE)	-2.43 (0.84)	-4.58 (0.93)	2.15 (-0.31, 4.61)
	Treatment P-value			0.08621
	Hedge's g (95% CI)			0.15 (-0.07, 0.37)
Female	N, n	63, 48	75, 45	
	Baseline Mean (SD)	66.50 (20.40)	70.31 (21.40)	
	Change from Baseline LS Mean (SE)	-3.37 (1.62)	-5.27 (1.68)	1.90 (-2.68, 6.49)
	Treatment P-value			0.41456
	Hedge's g (95% CI)			0.13 (-0.28, 0.53)
	Interaction P-value [b]			0.74853

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D.VAS.MM.S4.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EQ-5D VAS Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Region

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Western Europe	N, n	126, 85	129, 65	
	Baseline Mean (SD)	67.08 (18.66)	66.89 (20.92)	
	Change from Baseline LS Mean (SE)	-2.00 (1.21)	-6.66 (1.40)	4.66 (1.03, 8.30)
	Treatment P-value			0.01212
	Hedge's g (95% CI)			0.30 (-0.02, 0.62)
US	N, n	43, 28	44, 25	
	Baseline Mean (SD)	74.29 (20.23)	74.56 (15.52)	
	Change from Baseline LS Mean (SE)	-3.29 (2.16)	-1.65 (2.26)	-1.63 (-7.77, 4.50)
	Treatment P-value			0.60103
	Hedge's g (95% CI)			-0.15 (-0.68, 0.39)

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EQ5D.VAS.MM.S4.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EQ-5D VAS Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Region

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Rest of the World	N, n	132, 115	134, 102	
	Baseline Mean (SD)	67.63 (16.62)	72.14 (16.70)	
	Change from Baseline LS Mean (SE)	-3.03 (1.03)	-4.29 (1.10)	1.26 (-1.70, 4.23)
	Treatment P-value			0.40231
	Hedge's g (95% CI)			0.09 (-0.18, 0.35)
	Interaction P-value [b]			0.22358

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D.VAS.MM.S5.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EQ-5D VAS Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
0	N, n	120, 98	124, 89	
	Baseline Mean (SD)	73.10 (16.36)	75.17 (17.10)	
	Change from Baseline LS Mean (SE)	-4.73 (1.10)	-3.36 (1.16)	-1.38 (-4.51, 1.76)
	Treatment P-value			0.38767
	Hedge's g (95% CI)			-0.10 (-0.39, 0.18)
1	N, n	181, 130	183, 103	
	Baseline Mean (SD)	64.58 (18.24)	66.80 (18.37)	
	Change from Baseline LS Mean (SE)	-0.85 (0.99)	-5.92 (1.11)	5.07 (2.15, 7.99)
	Treatment P-value			0.00070
	Hedge's g (95% CI)			0.34 (0.08, 0.60)
	Interaction P-value [b]			0.00447

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D.VAS.MM.S6.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EQ-5D VAS Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Yes	N, n	93, 62	95, 51	
	Baseline Mean (SD)	63.44 (18.77)	69.04 (18.44)	
	Change from Baseline LS Mean (SE)	-0.78 (1.42)	-5.77 (1.60)	4.99 (0.78, 9.20)
	Treatment P-value			0.02025
	Hedge's g (95% CI)			0.30 (-0.07, 0.67)
No	N, n	208, 166	212, 141	
	Baseline Mean (SD)	70.04 (17.32)	71.27 (18.19)	
	Change from Baseline LS Mean (SE)	-3.28 (0.87)	-4.36 (0.94)	1.08 (-1.44, 3.61)
	Treatment P-value			0.39939
	Hedge's g (95% CI)			0.08 (-0.14, 0.30)
	Interaction P-value [b]			0.57000

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D.VAS.MM.S7.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EQ-5D VAS Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Paclitaxel	N, n	141, 117	112, 73	
	Baseline Mean (SD)	65.99 (18.82)	75.60 (14.86)	
	Change from Baseline LS Mean (SE)	-1.88 (1.03)	-6.04 (1.30)	4.17 (0.91, 7.43)
	Treatment P-value			0.01238
	Hedge's g (95% CI)			0.28 (-0.01, 0.57)
Docetaxel	N, n	87, 59	117, 72	
	Baseline Mean (SD)	72.34 (16.09)	70.94 (17.05)	
	Change from Baseline LS Mean (SE)	-4.20 (1.45)	-3.72 (1.34)	-0.47 (-4.35, 3.40)
	Treatment P-value			0.81054
	Hedge's g (95% CI)			-0.04 (-0.38, 0.31)

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D.VAS.MM.S7.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EQ-5D VAS Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Vinflunine	N, n	73, 52	78, 47	
	Baseline Mean (SD)	68.67 (17.29)	62.62 (21.93)	
	Change from Baseline LS Mean (SE)	-2.47 (1.59)	-4.03 (1.66)	1.56 (-2.94, 6.07)
	Treatment P-value			0.49609
	Hedge's g (95% CI)			0.10 (-0.29, 0.49)
	Interaction P-value [b]			0.76649

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D.VAS.MM.S8.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EQ-5D VAS Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Primary Site of Tumor

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Upper Tract	N, n	98, 75	107, 75	
	Baseline Mean (SD)	64.73 (18.78)	71.56 (15.74)	
	Change from Baseline LS Mean (SE)	-1.72 (1.28)	-4.90 (1.29)	3.17 (-0.39, 6.74)
	Treatment P-value			0.08108
	Hedge's g (95% CI)			0.20 (-0.11, 0.52)
Other	N, n	203, 153	200, 117	
	Baseline Mean (SD)	69.97 (17.30)	70.11 (19.71)	
	Change from Baseline LS Mean (SE)	-3.11 (0.91)	-4.62 (1.04)	1.51 (-1.22, 4.23)
	Treatment P-value			0.27710
	Hedge's g (95% CI)			0.11 (-0.13, 0.35)
	Interaction P-value [b]			0.91227

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D.VAS.MM.S9.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EQ-5D VAS Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
1-2 lines	N, n	262, 199	270, 166	
	Baseline Mean (SD)	67.68 (17.97)	70.64 (18.51)	
	Change from Baseline LS Mean (SE)	-2.62 (0.80)	-5.14 (0.87)	2.52 (0.19, 4.85)
	Treatment P-value			0.03397
	Hedge's g (95% CI)			0.17 (-0.03, 0.38)
>=3 lines	N, n	39, 29	37, 26	
	Baseline Mean (SD)	72.14 (17.41)	70.88 (16.65)	
	Change from Baseline LS Mean (SE)	-2.61 (2.00)	-2.05 (2.22)	-0.55 (-6.43, 5.32)
	Treatment P-value			0.85284
	Hedge's g (95% CI)			-0.04 (-0.57, 0.48)
	Interaction P-value [b]			0.47746

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EQ5D.VAS.MM.S10.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EQ-5D VAS Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Best Response to Prior CPI

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Responder	N, n	61, 49	50, 31	
	Baseline Mean (SD)	71.33 (15.41)	71.35 (17.75)	
	Change from Baseline LS Mean (SE)	-5.06 (1.60)	-6.50 (2.00)	1.45 (-3.59, 6.48)
	Treatment P-value			0.57284
	Hedge's g (95% CI)			0.11 (-0.34, 0.55)
Non-responder	N, n	207, 153	215, 135	
	Baseline Mean (SD)	67.84 (18.15)	70.57 (18.74)	
	Change from Baseline LS Mean (SE)	-1.86 (0.92)	-4.76 (0.99)	2.90 (0.24, 5.57)
	Treatment P-value			0.03261
	Hedge's g (95% CI)			0.19 (-0.04, 0.43)
	Interaction P-value [b]			0.96182

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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3 Gesundheitsbezogene Lebensqualität

3.1 Subgruppenanalysen zur gesundheitsbezogenen Lebensqualität gemäß EORTC QLQ-C30

3.1.1 Primäranalyse (MID ≥ 10 Punkte)

3.1.1.1 Globaler Gesundheitsstatus

Astellas: 7465-CL-0301
Table EORTC10.QL.KM.S1.FAS: EORTC Global Health Status: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	58 (53.7)	43 (38.7)
	Median Survival Est. (95% CI)	1.45 (0.82, 2.17)	2.17 (0.99, 5.36)
	Hazard Ratio (95% CI)		1.163 (0.784, 1.726)
	Treatment P-value [a]		0.46600
	Interaction P-value [b]		0.02056
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.35 (0.24, 0.45)	5, 0.31 (0.16, 0.47)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.QL.KM.S1.FAS: EORTC Global Health Status: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	104 (53.9)	113 (57.7)
	Median Survival Est. (95% CI)	1.41 (1.02, 1.94)	0.95 (0.62, 1.12)
	Hazard Ratio (95% CI)		0.662 (0.507, 0.865)
	Treatment P-value [a]		0.00259
	Interaction P-value [b]		0.02056
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.24 (0.16, 0.33)	6, 0.17 (0.11, 0.25)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.18 (0.10, 0.29)	1, 0.12 (0.04, 0.24)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.18 (0.10, 0.29)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.QL.KM.S2.FAS: EORTC Global Health Status: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	134 (53.8)	115 (48.1)
	Median Survival Est. (95% CI)	1.51 (1.05, 2.14)	1.02 (0.79, 1.68)
	Hazard Ratio (95% CI)		0.805 (0.627, 1.033)
	Treatment P-value [a]		0.08586
	Interaction P-value [b]		0.85297
6 Months	Patients at Risk, Survival Est. (95% CI)	18, 0.28 (0.20, 0.36)	8, 0.22 (0.14, 0.32)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.18 (0.10, 0.28)	0
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.18 (0.10, 0.28)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.QL.KM.S2.FAS: EORTC Global Health Status: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	28 (53.8)	41 (60.3)
	Median Survival Est. (95% CI)	1.02 (0.56, 1.54)	0.99 (0.56, 1.22)
	Hazard Ratio (95% CI)		0.847 (0.524, 1.370)
	Treatment P-value [a]		0.49670
	Interaction P-value [b]		0.85297
6 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.20 (0.06, 0.41)	3, 0.20 (0.10, 0.32)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.20 (0.10, 0.32)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.QL.KM.S3.FAS: EORTC Global Health Status: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	130 (54.6)	115 (49.6)
	Median Survival Est. (95% CI)	1.22 (0.95, 1.81)	0.99 (0.76, 1.28)
	Hazard Ratio (95% CI)		0.833 (0.648, 1.071)
	Treatment P-value [a]		0.17759
	Interaction P-value [b]		0.47947
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.27 (0.20, 0.35)	8, 0.24 (0.16, 0.33)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.17 (0.09, 0.27)	1, 0.14 (0.04, 0.30)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.17 (0.09, 0.27)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.QL.KM.S3.FAS: EORTC Global Health Status: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	32 (50.8)	41 (54.7)
	Median Survival Est. (95% CI)	2.17 (1.02, 5.52)	0.99 (0.76, 1.77)
	Hazard Ratio (95% CI)		0.689 (0.434, 1.095)
	Treatment P-value [a]		0.07094
	Interaction P-value [b]		0.47947
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.22 (0.08, 0.41)	3, 0.15 (0.05, 0.29)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.QL.KM.S4.FAS: EORTC Global Health Status: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	55 (43.7)	56 (43.4)
	Median Survival Est. (95% CI)	1.81 (0.95, 5.36)	0.79 (0.36, 1.15)
	Hazard Ratio (95% CI)		0.658 (0.454, 0.956)
	Treatment P-value [a]		0.02969
	Interaction P-value [b]		0.31412
6 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.34 (0.21, 0.47)	5, 0.27 (0.17, 0.38)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.QL.KM.S4.FAS: EORTC Global Health Status: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	19 (44.2)	18 (40.9)
	Median Survival Est. (95% CI)	1.38 (0.53, 5.49)	2.17 (0.82, 2.69)
	Hazard Ratio (95% CI)		1.147 (0.601, 2.186)
	Treatment P-value [a]		0.57073
	Interaction P-value [b]		0.31412
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.26 (0.09, 0.47)	2, 0.27 (0.11, 0.46)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Table EORTC10.QL.KM.S4.FAS: EORTC Global Health Status: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	88 (66.7)	82 (61.2)
	Median Survival Est. (95% CI)	1.31 (0.99, 1.87)	0.99 (0.76, 1.38)
	Hazard Ratio (95% CI)		0.834 (0.617, 1.128)
	Treatment P-value [a]		0.18119
	Interaction P-value [b]		0.31412
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.22 (0.14, 0.32)	4, 0.17 (0.08, 0.29)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.11 (0.04, 0.21)	1, 0.06 (0.01, 0.22)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.11 (0.04, 0.21)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Table EORTC10.QL.KM.S5.FAS: EORTC Global Health Status: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	73 (60.8)	71 (57.3)
	Median Survival Est. (95% CI)	1.41 (0.99, 1.97)	1.02 (0.82, 1.68)
	Hazard Ratio (95% CI)		0.815 (0.587, 1.131)
	Treatment P-value [a]		0.18450
	Interaction P-value [b]		0.87901
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.28 (0.19, 0.39)	2, 0.19 (0.08, 0.33)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.13 (0.04, 0.27)	0
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.13 (0.04, 0.27)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.QL.KM.S5.FAS: EORTC Global Health Status: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	89 (49.2)	85 (46.4)
	Median Survival Est. (95% CI)	1.38 (0.85, 2.30)	0.99 (0.56, 1.25)
	Hazard Ratio (95% CI)		0.787 (0.585, 1.060)
	Treatment P-value [a]		0.12576
	Interaction P-value [b]		0.87901
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.25 (0.16, 0.35)	9, 0.24 (0.15, 0.33)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.20 (0.10, 0.31)	1, 0.21 (0.13, 0.31)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Astellas: 7465-CL-0301
Table EORTC10.QL.KM.S6.FAS: EORTC Global Health Status: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	43 (46.2)	43 (45.3)
	Median Survival Est. (95% CI)	1.74 (0.95, 6.34)	1.12 (0.56, 1.38)
	Hazard Ratio (95% CI)		0.653 (0.427, 0.998)
	Treatment P-value [a]		0.03853
	Interaction P-value [b]		0.27079
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.36 (0.22, 0.50)	1, 0.19 (0.09, 0.32)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Table EORTC10.QL.KM.S6.FAS: EORTC Global Health Status: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	119 (57.2)	113 (53.3)
	Median Survival Est. (95% CI)	1.41 (0.99, 1.87)	0.99 (0.76, 1.41)
	Hazard Ratio (95% CI)		0.862 (0.666, 1.116)
	Treatment P-value [a]		0.28181
	Interaction P-value [b]		0.27079
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.23 (0.15, 0.32)	10, 0.24 (0.16, 0.33)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.18 (0.10, 0.28)	1, 0.16 (0.07, 0.29)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.18 (0.10, 0.28)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Table EORTC10.QL.KM.S7.FAS: EORTC Global Health Status: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	80 (56.7)	56 (50.0)
	Median Survival Est. (95% CI)	1.25 (0.79, 2.10)	1.05 (0.53, 1.91)
	Hazard Ratio (95% CI)		0.858 (0.609, 1.207)
	Treatment P-value [a]		0.37033
	Interaction P-value [b]		0.84632
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.24 (0.14, 0.34)	5, 0.24 (0.13, 0.37)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.18 (0.09, 0.29)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.QL.KM.S7.FAS: EORTC Global Health Status: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	48 (55.2)	63 (53.8)
	Median Survival Est. (95% CI)	1.41 (0.82, 2.37)	0.99 (0.76, 1.38)
	Hazard Ratio (95% CI)		0.739 (0.507, 1.077)
	Treatment P-value [a]		0.11252
	Interaction P-value [b]		0.84632
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.29 (0.17, 0.42)	2, 0.17 (0.07, 0.30)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.16 (0.06, 0.32)	1, 0.17 (0.07, 0.30)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.16 (0.06, 0.32)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.QL.KM.S7.FAS: EORTC Global Health Status: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	34 (46.6)	37 (47.4)
	Median Survival Est. (95% CI)	1.74 (0.95, 5.95)	0.99 (0.56, 1.77)
	Hazard Ratio (95% CI)		0.790 (0.496, 1.258)
	Treatment P-value [a]		0.27775
	Interaction P-value [b]		0.84632
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.29 (0.12, 0.49)	4, 0.27 (0.15, 0.41)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Table EORTC10.QL.KM.S8.FAS: EORTC Global Health Status: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	54 (55.1)	67 (62.6)
	Median Survival Est. (95% CI)	1.22 (0.72, 1.54)	0.79 (0.39, 0.99)
	Hazard Ratio (95% CI)		0.683 (0.477, 0.979)
	Treatment P-value [a]		0.04663
	Interaction P-value [b]		0.25278
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.30 (0.19, 0.41)	3, 0.18 (0.09, 0.28)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.08 (0.01, 0.27)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.QL.KM.S8.FAS: EORTC Global Health Status: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	108 (53.2)	89 (44.5)
	Median Survival Est. (95% CI)	1.74 (1.02, 2.14)	1.22 (0.99, 1.97)
	Hazard Ratio (95% CI)		0.891 (0.673, 1.180)
	Treatment P-value [a]		0.42164
	Interaction P-value [b]		0.25278
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.24 (0.16, 0.34)	8, 0.26 (0.17, 0.36)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.18 (0.10, 0.30)	1, 0.23 (0.13, 0.34)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.18 (0.10, 0.30)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.QL.KM.S9.FAS: EORTC Global Health Status: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	141 (53.8)	139 (51.5)
	Median Survival Est. (95% CI)	1.38 (1.02, 1.91)	0.99 (0.76, 1.18)
	Hazard Ratio (95% CI)		0.774 (0.612, 0.979)
	Treatment P-value [a]		0.02942
	Interaction P-value [b]		0.46118
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.25 (0.18, 0.33)	9, 0.20 (0.14, 0.28)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.16 (0.08, 0.26)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.QL.KM.S9.FAS: EORTC Global Health Status: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	21 (53.8)	17 (45.9)
	Median Survival Est. (95% CI)	1.71 (0.76, 6.34)	2.17 (0.33, NC)
	Hazard Ratio (95% CI)		1.000 (0.527, 1.896)
	Treatment P-value [a]		0.96675
	Interaction P-value [b]		0.46118
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.35 (0.16, 0.56)	2, 0.35 (0.15, 0.56)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.12 (0.01, 0.38)	1, 0.35 (0.15, 0.56)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.12 (0.01, 0.38)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.QL.KM.S10.FAS: EORTC Global Health Status: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	38 (62.3)	29 (58.0)
	Median Survival Est. (95% CI)	1.18 (0.59, 1.71)	0.99 (0.62, 2.46)
	Hazard Ratio (95% CI)		0.907 (0.559, 1.471)
	Treatment P-value [a]		0.62508
	Interaction P-value [b]		0.57979
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.20 (0.07, 0.39)	3, 0.20 (0.07, 0.39)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.10 (0.01, 0.32)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.QL.KM.S10.FAS: EORTC Global Health Status: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	105 (50.7)	107 (49.8)
	Median Survival Est. (95% CI)	1.45 (0.95, 2.10)	1.02 (0.66, 1.25)
	Hazard Ratio (95% CI)		0.775 (0.592, 1.016)
	Treatment P-value [a]		0.07244
	Interaction P-value [b]		0.57979
6 Months	Patients at Risk, Survival Est. (95% CI)	14, 0.31 (0.22, 0.39)	6, 0.23 (0.15, 0.31)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.20 (0.11, 0.31)	1, 0.23 (0.15, 0.31)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.20 (0.11, 0.31)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

3.1.1.2 Körperliche Funktion

Astellas: 7465-CL-0301
Table EORTC10.PF.KM.S1.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	52 (48.1)	49 (44.1)
	Median Survival Est. (95% CI)	2.14 (1.02, 6.54)	2.00 (1.22, 2.83)
	Hazard Ratio (95% CI)		0.870 (0.589, 1.286)
	Treatment P-value [a]		0.42262
	Interaction P-value [b]		0.62912
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.42 (0.29, 0.55)	5, 0.26 (0.15, 0.39)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.PF.KM.S1.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	101 (52.3)	102 (52.0)
	Median Survival Est. (95% CI)	1.74 (1.22, 2.43)	1.18 (0.99, 1.54)
	Hazard Ratio (95% CI)		0.773 (0.586, 1.020)
	Treatment P-value [a]		0.07873
	Interaction P-value [b]		0.62912
6 Months	Patients at Risk, Survival Est. (95% CI)	18, 0.33 (0.24, 0.41)	9, 0.20 (0.13, 0.29)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.16 (0.05, 0.33)	2, 0.17 (0.09, 0.27)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.PF.KM.S2.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	129 (51.8)	116 (48.5)
	Median Survival Est. (95% CI)	1.91 (1.28, 2.79)	1.51 (1.02, 1.94)
	Hazard Ratio (95% CI)		0.796 (0.619, 1.025)
	Treatment P-value [a]		0.05148
	Interaction P-value [b]		0.84641
6 Months	Patients at Risk, Survival Est. (95% CI)	26, 0.36 (0.29, 0.44)	10, 0.21 (0.13, 0.29)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.09 (0.01, 0.27)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.PF.KM.S2.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	24 (46.2)	35 (51.5)
	Median Survival Est. (95% CI)	1.54 (0.53, NC)	1.18 (0.89, 1.68)
	Hazard Ratio (95% CI)		0.844 (0.498, 1.428)
	Treatment P-value [a]		0.59198
	Interaction P-value [b]		0.84641
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.35 (0.19, 0.52)	4, 0.27 (0.15, 0.41)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.35 (0.19, 0.52)	2, 0.27 (0.15, 0.41)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.PF.KM.S3.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	128 (53.8)	115 (49.6)
	Median Survival Est. (95% CI)	1.64 (1.02, 2.23)	1.48 (1.02, 1.71)
	Hazard Ratio (95% CI)		0.838 (0.650, 1.080)
	Treatment P-value [a]		0.16118
	Interaction P-value [b]		0.40113
6 Months	Patients at Risk, Survival Est. (95% CI)	24, 0.34 (0.27, 0.42)	9, 0.21 (0.14, 0.30)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.12 (0.04, 0.26)	1, 0.12 (0.05, 0.23)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.PF.KM.S3.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	25 (39.7)	36 (48.0)
	Median Survival Est. (95% CI)	5.42 (1.22, NC)	1.22 (0.82, 2.46)
	Hazard Ratio (95% CI)		0.657 (0.394, 1.095)
	Treatment P-value [a]		0.09187
	Interaction P-value [b]		0.40113
6 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.43 (0.25, 0.59)	5, 0.24 (0.12, 0.39)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.24 (0.12, 0.39)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.PF.KM.S4.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	55 (43.7)	48 (37.2)
	Median Survival Est. (95% CI)	1.91 (0.95, 5.52)	1.48 (0.99, 2.00)
	Hazard Ratio (95% CI)		0.933 (0.633, 1.375)
	Treatment P-value [a]		0.73699
	Interaction P-value [b]		0.60302
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.36 (0.24, 0.49)	6, 0.32 (0.20, 0.45)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.32 (0.20, 0.45)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.PF.KM.S4.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	19 (44.2)	17 (38.6)
	Median Survival Est. (95% CI)	2.23 (0.82, 10.97)	1.68 (0.99, 4.99)
	Hazard Ratio (95% CI)		0.841 (0.432, 1.637)
	Treatment P-value [a]		0.59437
	Interaction P-value [b]		0.60302
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.36 (0.17, 0.55)	2, 0.26 (0.08, 0.47)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.18 (0.02, 0.49)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.PF.KM.S4.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	79 (59.8)	86 (64.2)
	Median Survival Est. (95% CI)	1.71 (1.02, 5.36)	1.38 (0.99, 1.68)
	Hazard Ratio (95% CI)		0.726 (0.534, 0.987)
	Treatment P-value [a]		0.02708
	Interaction P-value [b]		0.60302
6 Months	Patients at Risk, Survival Est. (95% CI)	18, 0.36 (0.27, 0.46)	6, 0.17 (0.09, 0.26)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.17 (0.07, 0.29)	1, 0.04 (0.00, 0.17)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.PF.KM.S5.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	66 (55.0)	67 (54.0)
	Median Survival Est. (95% CI)	1.91 (1.25, 5.42)	1.68 (1.22, 2.37)
	Hazard Ratio (95% CI)		0.798 (0.568, 1.123)
	Treatment P-value [a]		0.15970
	Interaction P-value [b]		0.95021
6 Months	Patients at Risk, Survival Est. (95% CI)	15, 0.35 (0.24, 0.46)	6, 0.23 (0.13, 0.35)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.24 (0.14, 0.37)	1, 0.12 (0.03, 0.27)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.PF.KM.S5.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	87 (48.1)	84 (45.9)
	Median Survival Est. (95% CI)	1.84 (0.99, 5.36)	1.18 (0.95, 1.54)
	Hazard Ratio (95% CI)		0.810 (0.599, 1.095)
	Treatment P-value [a]		0.18148
	Interaction P-value [b]		0.95021
6 Months	Patients at Risk, Survival Est. (95% CI)	15, 0.37 (0.28, 0.47)	8, 0.21 (0.13, 0.31)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.09 (0.01, 0.28)	1, 0.18 (0.09, 0.28)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.PF.KM.S6.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	43 (46.2)	42 (44.2)
	Median Survival Est. (95% CI)	2.23 (0.89, 5.52)	1.12 (0.76, 1.54)
	Hazard Ratio (95% CI)		0.695 (0.452, 1.068)
	Treatment P-value [a]		0.13384
	Interaction P-value [b]		0.43331
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.37 (0.24, 0.50)	2, 0.21 (0.09, 0.38)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.27 (0.14, 0.41)	1, 0.21 (0.09, 0.38)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.PF.KM.S6.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	110 (52.9)	109 (51.4)
	Median Survival Est. (95% CI)	1.81 (1.22, 5.36)	1.61 (1.15, 1.94)
	Hazard Ratio (95% CI)		0.850 (0.652, 1.108)
	Treatment P-value [a]		0.22567
	Interaction P-value [b]		0.43331
6 Months	Patients at Risk, Survival Est. (95% CI)	19, 0.36 (0.27, 0.44)	12, 0.23 (0.15, 0.31)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.09 (0.01, 0.28)	1, 0.15 (0.08, 0.25)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.PF.KM.S7.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	83 (58.9)	52 (46.4)
	Median Survival Est. (95% CI)	1.12 (0.79, 2.14)	1.54 (1.18, 2.17)
	Hazard Ratio (95% CI)		1.046 (0.738, 1.481)
	Treatment P-value [a]		0.78654
	Interaction P-value [b]		0.04268
6 Months	Patients at Risk, Survival Est. (95% CI)	14, 0.32 (0.23, 0.42)	3, 0.22 (0.11, 0.36)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.13 (0.05, 0.26)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.PF.KM.S7.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	39 (44.8)	66 (56.4)
	Median Survival Est. (95% CI)	5.45 (1.41, 10.97)	1.18 (0.82, 1.94)
	Hazard Ratio (95% CI)		0.534 (0.357, 0.796)
	Treatment P-value [a]		0.00162
	Interaction P-value [b]		0.04268
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.44 (0.30, 0.57)	6, 0.15 (0.07, 0.26)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.18 (0.02, 0.48)	1, 0.04 (0.00, 0.16)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Table EORTC10.PF.KM.S7.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	31 (42.5)	33 (42.3)
	Median Survival Est. (95% CI)	2.43 (1.25, 5.52)	1.51 (0.79, 2.73)
	Hazard Ratio (95% CI)		0.854 (0.523, 1.395)
	Treatment P-value [a]		0.46640
	Interaction P-value [b]		0.04268
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.32 (0.16, 0.50)	5, 0.36 (0.22, 0.49)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.36 (0.22, 0.49)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Astellas: 7465-CL-0301
Table EORTC10.PF.KM.S8.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	53 (54.1)	59 (55.1)
	Median Survival Est. (95% CI)	1.54 (1.12, 5.36)	1.45 (0.99, 1.94)
	Hazard Ratio (95% CI)		0.858 (0.591, 1.245)
	Treatment P-value [a]		0.34464
	Interaction P-value [b]		0.69995
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.34 (0.22, 0.46)	4, 0.24 (0.13, 0.36)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.11 (0.03, 0.24)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.PF.KM.S8.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	100 (49.3)	92 (46.0)
	Median Survival Est. (95% CI)	1.91 (1.05, 5.42)	1.45 (1.02, 2.00)
	Hazard Ratio (95% CI)		0.783 (0.589, 1.041)
	Treatment P-value [a]		0.10372
	Interaction P-value [b]		0.69995
6 Months	Patients at Risk, Survival Est. (95% CI)	19, 0.37 (0.28, 0.45)	10, 0.22 (0.14, 0.31)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.13 (0.02, 0.38)	2, 0.17 (0.09, 0.27)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.PF.KM.S9.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	132 (50.4)	134 (49.6)
	Median Survival Est. (95% CI)	1.91 (1.22, 2.79)	1.38 (0.99, 1.68)
	Hazard Ratio (95% CI)		0.755 (0.592, 0.962)
	Treatment P-value [a]		0.02223
	Interaction P-value [b]		0.16689
6 Months	Patients at Risk, Survival Est. (95% CI)	28, 0.36 (0.28, 0.44)	11, 0.20 (0.13, 0.28)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.15 (0.05, 0.31)	1, 0.13 (0.06, 0.22)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.PF.KM.S9.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	21 (53.8)	17 (45.9)
	Median Survival Est. (95% CI)	1.71 (0.69, 6.44)	1.68 (1.18, NC)
	Hazard Ratio (95% CI)		1.224 (0.645, 2.324)
	Treatment P-value [a]		0.57632
	Interaction P-value [b]		0.16689
6 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.33 (0.15, 0.53)	3, 0.40 (0.22, 0.58)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.40 (0.22, 0.58)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.PF.KM.S10.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	36 (59.0)	29 (58.0)
	Median Survival Est. (95% CI)	1.41 (0.79, 2.66)	1.45 (0.59, 2.17)
	Hazard Ratio (95% CI)		0.816 (0.500, 1.331)
	Treatment P-value [a]		0.45682
	Interaction P-value [b]		0.98468
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.28 (0.14, 0.43)	3, 0.24 (0.11, 0.40)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.PF.KM.S10.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	99 (47.8)	102 (47.4)
	Median Survival Est. (95% CI)	2.00 (1.02, 5.42)	1.45 (1.02, 1.94)
	Hazard Ratio (95% CI)		0.811 (0.614, 1.072)
	Treatment P-value [a]		0.13590
	Interaction P-value [b]		0.98468
6 Months	Patients at Risk, Survival Est. (95% CI)	22, 0.40 (0.32, 0.49)	10, 0.22 (0.14, 0.31)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.21 (0.12, 0.32)	2, 0.16 (0.08, 0.26)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

3.1.1.3 Rollenfunktion

Astellas: 7465-CL-0301
Table EORTC10.RF.KM.S1.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	61 (56.5)	57 (51.4)
	Median Survival Est. (95% CI)	1.05 (0.79, 2.14)	1.05 (0.72, 1.71)
	Hazard Ratio (95% CI)		0.845 (0.589, 1.213)
	Treatment P-value [a]		0.36270
	Interaction P-value [b]		0.54084
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.28 (0.17, 0.40)	5, 0.20 (0.10, 0.31)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.RF.KM.S1.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	113 (58.5)	118 (60.2)
	Median Survival Est. (95% CI)	0.92 (0.72, 1.38)	0.76 (0.53, 0.95)
	Hazard Ratio (95% CI)		0.736 (0.568, 0.953)
	Treatment P-value [a]		0.02203
	Interaction P-value [b]		0.54084
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.21 (0.14, 0.30)	7, 0.14 (0.08, 0.21)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.RF.KM.S2.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	139 (55.8)	132 (55.2)
	Median Survival Est. (95% CI)	1.25 (0.89, 1.91)	0.79 (0.69, 1.02)
	Hazard Ratio (95% CI)		0.707 (0.557, 0.898)
	Treatment P-value [a]		0.00468
	Interaction P-value [b]		0.01491
6 Months	Patients at Risk, Survival Est. (95% CI)	19, 0.27 (0.19, 0.35)	10, 0.17 (0.11, 0.25)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.RF.KM.S2.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	35 (67.3)	43 (63.2)
	Median Survival Est. (95% CI)	0.56 (0.33, 0.79)	0.76 (0.53, 1.15)
	Hazard Ratio (95% CI)		1.328 (0.849, 2.075)
	Treatment P-value [a]		0.21193
	Interaction P-value [b]		0.01491
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.09 (0.02, 0.22)	2, 0.12 (0.04, 0.24)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.RF.KM.S3.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	140 (58.8)	127 (54.7)
	Median Survival Est. (95% CI)	0.99 (0.76, 1.38)	0.76 (0.62, 1.15)
	Hazard Ratio (95% CI)		0.855 (0.672, 1.087)
	Treatment P-value [a]		0.22704
	Interaction P-value [b]		0.08603
6 Months	Patients at Risk, Survival Est. (95% CI)	15, 0.23 (0.16, 0.31)	10, 0.19 (0.13, 0.27)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.RF.KM.S3.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	34 (54.0)	48 (64.0)
	Median Survival Est. (95% CI)	1.03 (0.56, 5.52)	0.82 (0.56, 1.02)
	Hazard Ratio (95% CI)		0.551 (0.354, 0.856)
	Treatment P-value [a]		0.00551
	Interaction P-value [b]		0.08603
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.27 (0.12, 0.43)	2, 0.05 (0.01, 0.15)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.RF.KM.S4.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	64 (50.8)	61 (47.3)
	Median Survival Est. (95% CI)	1.05 (0.72, 1.91)	0.72 (0.36, 0.99)
	Hazard Ratio (95% CI)		0.719 (0.506, 1.021)
	Treatment P-value [a]		0.08969
	Interaction P-value [b]		0.84350
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.25 (0.14, 0.37)	5, 0.20 (0.12, 0.30)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.RF.KM.S4.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	23 (53.5)	24 (54.5)
	Median Survival Est. (95% CI)	0.85 (0.53, 2.96)	0.82 (0.56, 1.12)
	Hazard Ratio (95% CI)		0.745 (0.420, 1.323)
	Treatment P-value [a]		0.24421
	Interaction P-value [b]		0.84350
6 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.18 (0.05, 0.37)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.RF.KM.S4.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	87 (65.9)	90 (67.2)
	Median Survival Est. (95% CI)	0.92 (0.76, 1.54)	0.82 (0.69, 1.22)
	Hazard Ratio (95% CI)		0.821 (0.611, 1.103)
	Treatment P-value [a]		0.18873
	Interaction P-value [b]		0.84350
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.24 (0.16, 0.34)	7, 0.16 (0.09, 0.26)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.RF.KM.S5.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	72 (60.0)	81 (65.3)
	Median Survival Est. (95% CI)	1.28 (0.85, 2.14)	0.82 (0.69, 1.22)
	Hazard Ratio (95% CI)		0.673 (0.489, 0.925)
	Treatment P-value [a]		0.00910
	Interaction P-value [b]		0.25085
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.28 (0.19, 0.39)	5, 0.15 (0.08, 0.25)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.RF.KM.S5.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	102 (56.4)	94 (51.4)
	Median Survival Est. (95% CI)	0.82 (0.59, 1.25)	0.76 (0.53, 0.99)
	Hazard Ratio (95% CI)		0.862 (0.652, 1.142)
	Treatment P-value [a]		0.32260
	Interaction P-value [b]		0.25085
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.20 (0.11, 0.30)	7, 0.16 (0.09, 0.25)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.RF.KM.S6.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	51 (54.8)	51 (53.7)
	Median Survival Est. (95% CI)	0.92 (0.72, 1.45)	0.59 (0.36, 0.95)
	Hazard Ratio (95% CI)		0.614 (0.415, 0.907)
	Treatment P-value [a]		0.01864
	Interaction P-value [b]		0.20116
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.22 (0.11, 0.34)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.RF.KM.S6.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	123 (59.1)	124 (58.5)
	Median Survival Est. (95% CI)	1.02 (0.76, 1.54)	0.82 (0.72, 1.18)
	Hazard Ratio (95% CI)		0.831 (0.647, 1.066)
	Treatment P-value [a]		0.15828
	Interaction P-value [b]		0.20116
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.24 (0.16, 0.33)	12, 0.18 (0.12, 0.26)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.RF.KM.S7.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	85 (60.3)	63 (56.3)
	Median Survival Est. (95% CI)	0.92 (0.62, 1.38)	0.82 (0.72, 1.45)
	Hazard Ratio (95% CI)		0.849 (0.612, 1.177)
	Treatment P-value [a]		0.35202
	Interaction P-value [b]		0.58316
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.25 (0.16, 0.35)	3, 0.16 (0.08, 0.26)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.RF.KM.S7.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	49 (56.3)	72 (61.5)
	Median Survival Est. (95% CI)	0.89 (0.62, 1.87)	0.76 (0.43, 1.02)
	Hazard Ratio (95% CI)		0.664 (0.462, 0.955)
	Treatment P-value [a]		0.02967
	Interaction P-value [b]		0.58316
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.24 (0.13, 0.37)	5, 0.12 (0.05, 0.22)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.RF.KM.S7.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	40 (54.8)	40 (51.3)
	Median Survival Est. (95% CI)	1.28 (0.79, 2.79)	0.79 (0.53, 1.38)
	Hazard Ratio (95% CI)		0.827 (0.533, 1.282)
	Treatment P-value [a]		0.42127
	Interaction P-value [b]		0.58316
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.22 (0.10, 0.37)	4, 0.24 (0.13, 0.36)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.RF.KM.S8.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	54 (55.1)	75 (70.1)
	Median Survival Est. (95% CI)	0.92 (0.59, 1.45)	0.72 (0.53, 0.99)
	Hazard Ratio (95% CI)		0.654 (0.460, 0.929)
	Treatment P-value [a]		0.01890
	Interaction P-value [b]		0.22321
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.31 (0.20, 0.43)	4, 0.11 (0.04, 0.20)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.RF.KM.S8.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	120 (59.1)	100 (50.0)
	Median Survival Est. (95% CI)	1.02 (0.76, 1.45)	0.95 (0.72, 1.22)
	Hazard Ratio (95% CI)		0.859 (0.659, 1.121)
	Treatment P-value [a]		0.27543
	Interaction P-value [b]		0.22321
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.20 (0.13, 0.29)	8, 0.19 (0.12, 0.28)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.RF.KM.S9.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	150 (57.3)	152 (56.3)
	Median Survival Est. (95% CI)	0.99 (0.76, 1.38)	0.76 (0.59, 0.99)
	Hazard Ratio (95% CI)		0.744 (0.594, 0.933)
	Treatment P-value [a]		0.01189
	Interaction P-value [b]		0.40581
6 Months	Patients at Risk, Survival Est. (95% CI)	19, 0.25 (0.18, 0.32)	10, 0.16 (0.11, 0.23)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.RF.KM.S9.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	24 (61.5)	23 (62.2)
	Median Survival Est. (95% CI)	1.08 (0.49, 5.36)	0.95 (0.76, 2.56)
	Hazard Ratio (95% CI)		0.966 (0.545, 1.713)
	Treatment P-value [a]		0.76684
	Interaction P-value [b]		0.40581
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.16 (0.03, 0.37)	2, 0.15 (0.03, 0.34)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.RF.KM.S10.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	38 (62.3)	33 (66.0)
	Median Survival Est. (95% CI)	1.18 (0.56, 2.14)	0.97 (0.39, 1.51)
	Hazard Ratio (95% CI)		0.834 (0.522, 1.331)
	Treatment P-value [a]		0.47731
	Interaction P-value [b]		0.62344
6 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.16 (0.04, 0.35)	5, 0.23 (0.11, 0.38)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.RF.KM.S10.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	111 (53.6)	119 (55.3)
	Median Survival Est. (95% CI)	0.99 (0.76, 1.45)	0.76 (0.66, 1.02)
	Hazard Ratio (95% CI)		0.729 (0.562, 0.946)
	Treatment P-value [a]		0.01770
	Interaction P-value [b]		0.62344
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.29 (0.21, 0.38)	7, 0.14 (0.08, 0.22)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

3.1.1.4 Emotionale Funktion

Astellas: 7465-CL-0301
Table EORTC10.EF.KM.S1.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	45 (41.7)	40 (36.0)
	Median Survival Est. (95% CI)	3.75 (1.48, 7.56)	2.83 (2.17, 7.69)
	Hazard Ratio (95% CI)		1.039 (0.678, 1.591)
	Treatment P-value [a]		0.83599
	Interaction P-value [b]		0.08045
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.45 (0.32, 0.58)	10, 0.37 (0.23, 0.50)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.EF.KM.S1.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	71 (36.8)	84 (42.9)
	Median Survival Est. (95% CI)	5.45 (2.20, NC)	1.61 (1.05, 4.17)
	Hazard Ratio (95% CI)		0.647 (0.471, 0.888)
	Treatment P-value [a]		0.00816
	Interaction P-value [b]		0.08045
6 Months	Patients at Risk, Survival Est. (95% CI)	18, 0.41 (0.30, 0.51)	11, 0.36 (0.27, 0.46)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.20 (0.02, 0.52)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Table EORTC10.EF.KM.S2.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	100 (40.2)	91 (38.1)
	Median Survival Est. (95% CI)	5.42 (2.43, 6.54)	2.63 (1.68, 5.32)
	Hazard Ratio (95% CI)		0.819 (0.616, 1.088)
	Treatment P-value [a]		0.17604
	Interaction P-value [b]		0.40837
6 Months	Patients at Risk, Survival Est. (95% CI)	26, 0.42 (0.32, 0.50)	18, 0.40 (0.31, 0.48)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.16 (0.02, 0.43)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.EF.KM.S2.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	16 (30.8)	33 (48.5)
	Median Survival Est. (95% CI)	5.52 (0.76, NC)	1.28 (0.99, 2.69)
	Hazard Ratio (95% CI)		0.619 (0.340, 1.126)
	Treatment P-value [a]		0.14528
	Interaction P-value [b]		0.40837
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.47 (0.22, 0.68)	3, 0.27 (0.13, 0.43)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.EF.KM.S3.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	91 (38.2)	96 (41.4)
	Median Survival Est. (95% CI)	5.42 (2.43, 7.16)	2.37 (1.45, 4.34)
	Hazard Ratio (95% CI)		0.750 (0.563, 0.999)
	Treatment P-value [a]		0.04956
	Interaction P-value [b]		0.75254
6 Months	Patients at Risk, Survival Est. (95% CI)	23, 0.44 (0.34, 0.53)	16, 0.35 (0.26, 0.44)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.17 (0.02, 0.45)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Table EORTC10.EF.KM.S3.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	25 (39.7)	28 (37.3)
	Median Survival Est. (95% CI)	5.52 (1.48, NC)	2.43 (1.08, NC)
	Hazard Ratio (95% CI)		0.827 (0.482, 1.420)
	Treatment P-value [a]		0.54745
	Interaction P-value [b]		0.75254
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.38 (0.21, 0.56)	5, 0.40 (0.25, 0.54)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.EF.KM.S4.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	39 (31.0)	47 (36.4)
	Median Survival Est. (95% CI)	5.52 (2.66, NC)	1.97 (1.08, 2.63)
	Hazard Ratio (95% CI)		0.616 (0.403, 0.942)
	Treatment P-value [a]		0.02480
	Interaction P-value [b]		0.45136
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.45 (0.30, 0.59)	7, 0.34 (0.23, 0.46)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.EF.KM.S4.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	12 (27.9)	13 (29.5)
	Median Survival Est. (95% CI)	5.45 (1.45, NC)	2.69 (0.85, NC)
	Hazard Ratio (95% CI)		0.874 (0.399, 1.917)
	Treatment P-value [a]		0.82402
	Interaction P-value [b]		0.45136
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.49 (0.24, 0.70)	3, 0.43 (0.21, 0.63)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.EF.KM.S4.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	65 (49.2)	64 (47.8)
	Median Survival Est. (95% CI)	2.63 (1.64, 5.95)	2.83 (1.22, 5.39)
	Hazard Ratio (95% CI)		0.865 (0.612, 1.222)
	Treatment P-value [a]		0.35984
	Interaction P-value [b]		0.45136
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.39 (0.28, 0.49)	11, 0.37 (0.26, 0.48)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.26 (0.13, 0.40)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.EF.KM.S5.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	50 (41.7)	49 (39.5)
	Median Survival Est. (95% CI)	5.52 (1.87, NC)	4.86 (1.97, NC)
	Hazard Ratio (95% CI)		0.892 (0.601, 1.323)
	Treatment P-value [a]		0.55202
	Interaction P-value [b]		0.30930
6 Months	Patients at Risk, Survival Est. (95% CI)	16, 0.45 (0.33, 0.57)	11, 0.46 (0.34, 0.58)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.39 (0.26, 0.52)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.EF.KM.S5.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	66 (36.5)	75 (41.0)
	Median Survival Est. (95% CI)	5.42 (2.14, 7.16)	1.48 (1.05, 2.63)
	Hazard Ratio (95% CI)		0.683 (0.490, 0.951)
	Treatment P-value [a]		0.02236
	Interaction P-value [b]		0.30930
6 Months	Patients at Risk, Survival Est. (95% CI)	14, 0.40 (0.28, 0.51)	10, 0.28 (0.19, 0.39)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.EF.KM.S6.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	31 (33.3)	37 (38.9)
	Median Survival Est. (95% CI)	5.49 (2.20, NC)	1.28 (0.85, 2.63)
	Hazard Ratio (95% CI)		0.559 (0.346, 0.902)
	Treatment P-value [a]		0.01411
	Interaction P-value [b]		0.13473
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.41 (0.25, 0.57)	1, 0.28 (0.14, 0.43)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.EF.KM.S6.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	85 (40.9)	87 (41.0)
	Median Survival Est. (95% CI)	5.45 (1.94, 7.56)	2.83 (1.68, 5.39)
	Hazard Ratio (95% CI)		0.860 (0.638, 1.160)
	Treatment P-value [a]		0.32669
	Interaction P-value [b]		0.13473
6 Months	Patients at Risk, Survival Est. (95% CI)	21, 0.43 (0.33, 0.52)	20, 0.39 (0.30, 0.49)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.17 (0.02, 0.45)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.EF.KM.S7.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	56 (39.7)	38 (33.9)
	Median Survival Est. (95% CI)	5.39 (2.43, 7.56)	4.17 (1.68, 8.77)
	Hazard Ratio (95% CI)		0.951 (0.630, 1.437)
	Treatment P-value [a]		0.81338
	Interaction P-value [b]		0.34611
6 Months	Patients at Risk, Survival Est. (95% CI)	15, 0.41 (0.29, 0.53)	7, 0.47 (0.34, 0.59)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.30 (0.16, 0.45)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.EF.KM.S7.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	38 (43.7)	53 (45.3)
	Median Survival Est. (95% CI)	1.94 (1.48, NC)	1.94 (0.95, 5.32)
	Hazard Ratio (95% CI)		0.785 (0.517, 1.191)
	Treatment P-value [a]		0.24075
	Interaction P-value [b]		0.34611
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.40 (0.26, 0.54)	9, 0.30 (0.18, 0.43)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.EF.KM.S7.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	22 (30.1)	33 (42.3)
	Median Survival Est. (95% CI)	5.95 (2.14, NC)	1.97 (0.99, 4.34)
	Hazard Ratio (95% CI)		0.574 (0.335, 0.986)
	Treatment P-value [a]		0.05146
	Interaction P-value [b]		0.34611
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.47 (0.26, 0.65)	5, 0.33 (0.20, 0.47)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.EF.KM.S8.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	41 (41.8)	48 (44.9)
	Median Survival Est. (95% CI)	5.42 (1.41, 7.16)	2.46 (0.99, 8.77)
	Hazard Ratio (95% CI)		0.892 (0.588, 1.355)
	Treatment P-value [a]		0.62359
	Interaction P-value [b]		0.40300
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.44 (0.30, 0.56)	10, 0.39 (0.27, 0.51)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Table EORTC10.EF.KM.S8.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	75 (36.9)	76 (38.0)
	Median Survival Est. (95% CI)	5.45 (2.63, 8.38)	2.37 (1.45, 4.17)
	Hazard Ratio (95% CI)		0.713 (0.518, 0.981)
	Treatment P-value [a]		0.04006
	Interaction P-value [b]		0.40300
6 Months	Patients at Risk, Survival Est. (95% CI)	19, 0.41 (0.30, 0.51)	11, 0.35 (0.25, 0.45)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.19 (0.02, 0.49)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.EF.KM.S9.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	101 (38.5)	106 (39.3)
	Median Survival Est. (95% CI)	5.45 (2.20, 7.16)	2.37 (1.48, 4.34)
	Hazard Ratio (95% CI)		0.784 (0.597, 1.030)
	Treatment P-value [a]		0.08319
	Interaction P-value [b]		0.67932
6 Months	Patients at Risk, Survival Est. (95% CI)	28, 0.42 (0.33, 0.51)	20, 0.38 (0.30, 0.46)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.18 (0.02, 0.47)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.EF.KM.S9.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	15 (38.5)	18 (48.6)
	Median Survival Est. (95% CI)	5.42 (1.64, NC)	2.43 (0.95, NC)
	Hazard Ratio (95% CI)		0.671 (0.338, 1.333)
	Treatment P-value [a]		0.21102
	Interaction P-value [b]		0.67932
6 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.43 (0.20, 0.64)	1, 0.19 (0.02, 0.50)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.EF.KM.S10.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	33 (54.1)	25 (50.0)
	Median Survival Est. (95% CI)	1.91 (1.22, 5.45)	2.17 (0.99, NC)
	Hazard Ratio (95% CI)		1.016 (0.604, 1.708)
	Treatment P-value [a]		0.86911
	Interaction P-value [b]		0.22083
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.27 (0.12, 0.44)	5, 0.40 (0.24, 0.55)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.EF.KM.S10.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	69 (33.3)	82 (38.1)
	Median Survival Est. (95% CI)	5.52 (3.32, NC)	2.63 (1.38, 4.34)
	Hazard Ratio (95% CI)		0.693 (0.503, 0.956)
	Treatment P-value [a]		0.02883
	Interaction P-value [b]		0.22083
6 Months	Patients at Risk, Survival Est. (95% CI)	23, 0.48 (0.37, 0.57)	15, 0.37 (0.28, 0.47)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.41 (0.29, 0.53)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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3.1.1.5 Kognitive Funktion

Astellas: 7465-CL-0301
Table EORTC10.CF.KM.S1.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	53 (49.1)	47 (42.3)
	Median Survival Est. (95% CI)	2.07 (0.99, 5.36)	1.61 (1.02, 4.37)
	Hazard Ratio (95% CI)		1.008 (0.680, 1.493)
	Treatment P-value [a]		0.94994
	Interaction P-value [b]		0.58481
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.34 (0.22, 0.47)	6, 0.34 (0.22, 0.46)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.CF.KM.S1.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	102 (52.8)	96 (49.0)
	Median Survival Est. (95% CI)	1.68 (1.08, 1.94)	1.22 (0.79, 1.54)
	Hazard Ratio (95% CI)		0.881 (0.667, 1.164)
	Treatment P-value [a]		0.39122
	Interaction P-value [b]		0.58481
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.25 (0.16, 0.34)	9, 0.32 (0.24, 0.40)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.25 (0.16, 0.34)	2, 0.17 (0.07, 0.32)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.CF.KM.S2.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	130 (52.2)	113 (47.3)
	Median Survival Est. (95% CI)	1.71 (1.22, 2.20)	1.31 (0.95, 1.68)
	Hazard Ratio (95% CI)		0.871 (0.677, 1.121)
	Treatment P-value [a]		0.28612
	Interaction P-value [b]		0.37313
6 Months	Patients at Risk, Survival Est. (95% CI)	14, 0.29 (0.21, 0.37)	11, 0.31 (0.23, 0.39)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.CF.KM.S2.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	25 (48.1)	30 (44.1)
	Median Survival Est. (95% CI)	1.51 (0.56, 5.32)	1.51 (1.05, NC)
	Hazard Ratio (95% CI)		1.138 (0.669, 1.935)
	Treatment P-value [a]		0.60411
	Interaction P-value [b]		0.37313
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.25 (0.10, 0.43)	4, 0.37 (0.23, 0.51)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.25 (0.10, 0.43)	2, 0.37 (0.23, 0.51)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.CF.KM.S3.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	120 (50.4)	111 (47.8)
	Median Survival Est. (95% CI)	1.68 (1.02, 2.14)	1.45 (0.82, 1.68)
	Hazard Ratio (95% CI)		0.865 (0.668, 1.119)
	Treatment P-value [a]		0.27309
	Interaction P-value [b]		0.31762
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.32 (0.24, 0.40)	11, 0.30 (0.22, 0.39)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.21 (0.11, 0.33)	1, 0.12 (0.03, 0.26)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.CF.KM.S3.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	35 (55.6)	32 (42.7)
	Median Survival Est. (95% CI)	1.97 (1.02, 3.58)	1.45 (1.02, NC)
	Hazard Ratio (95% CI)		1.142 (0.706, 1.844)
	Treatment P-value [a]		0.69947
	Interaction P-value [b]		0.31762
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.11 (0.01, 0.33)	4, 0.38 (0.25, 0.51)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.38 (0.25, 0.51)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.CF.KM.S4.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	53 (42.1)	48 (37.2)
	Median Survival Est. (95% CI)	1.77 (0.99, 5.49)	1.08 (0.76, 6.51)
	Hazard Ratio (95% CI)		0.897 (0.607, 1.326)
	Treatment P-value [a]		0.62390
	Interaction P-value [b]		0.83428
6 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.35 (0.21, 0.49)	6, 0.40 (0.29, 0.51)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.27 (0.12, 0.44)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.CF.KM.S4.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	14 (32.6)	15 (34.1)
	Median Survival Est. (95% CI)	2.63 (1.51, NC)	1.94 (0.79, NC)
	Hazard Ratio (95% CI)		0.780 (0.376, 1.617)
	Treatment P-value [a]		0.58571
	Interaction P-value [b]		0.83428
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.42 (0.22, 0.61)	2, 0.40 (0.21, 0.59)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.42 (0.22, 0.61)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.CF.KM.S4.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	88 (66.7)	80 (59.7)
	Median Survival Est. (95% CI)	1.28 (0.95, 1.91)	1.28 (0.95, 1.64)
	Hazard Ratio (95% CI)		0.978 (0.723, 1.324)
	Treatment P-value [a]		0.87063
	Interaction P-value [b]		0.83428
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.21 (0.12, 0.31)	7, 0.26 (0.17, 0.36)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.08 (0.01, 0.26)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.CF.KM.S5.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	66 (55.0)	62 (50.0)
	Median Survival Est. (95% CI)	1.77 (1.08, 5.32)	1.61 (1.22, 3.78)
	Hazard Ratio (95% CI)		0.995 (0.703, 1.408)
	Treatment P-value [a]		0.87554
	Interaction P-value [b]		0.53794
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.32 (0.21, 0.43)	7, 0.35 (0.25, 0.46)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.18 (0.06, 0.35)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.CF.KM.S5.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	89 (49.2)	81 (44.3)
	Median Survival Est. (95% CI)	1.51 (0.99, 2.20)	0.99 (0.76, 1.51)
	Hazard Ratio (95% CI)		0.861 (0.637, 1.164)
	Treatment P-value [a]		0.32925
	Interaction P-value [b]		0.53794
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.25 (0.16, 0.36)	8, 0.30 (0.21, 0.39)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.22 (0.12, 0.33)	1, 0.19 (0.07, 0.34)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Astellas: 7465-CL-0301
Table EORTC10.CF.KM.S6.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	46 (49.5)	42 (44.2)
	Median Survival Est. (95% CI)	1.31 (0.76, 2.69)	1.28 (0.62, 1.54)
	Hazard Ratio (95% CI)		0.888 (0.585, 1.350)
	Treatment P-value [a]		0.58275
	Interaction P-value [b]		0.83985
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.29 (0.17, 0.42)	2, 0.25 (0.14, 0.38)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.12 (0.02, 0.28)	1, 0.25 (0.14, 0.38)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Astellas: 7465-CL-0301
Table EORTC10.CF.KM.S6.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	109 (52.4)	101 (47.6)
	Median Survival Est. (95% CI)	1.77 (1.41, 2.43)	1.45 (1.02, 2.37)
	Hazard Ratio (95% CI)		0.935 (0.713, 1.226)
	Treatment P-value [a]		0.63970
	Interaction P-value [b]		0.83985
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.28 (0.19, 0.37)	13, 0.35 (0.26, 0.43)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.17 (0.07, 0.31)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.CF.KM.S7.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	86 (61.0)	50 (44.6)
	Median Survival Est. (95% CI)	1.08 (0.82, 1.74)	1.51 (1.18, 3.78)
	Hazard Ratio (95% CI)		1.299 (0.916, 1.841)
	Treatment P-value [a]		0.13385
	Interaction P-value [b]		0.03084
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.16 (0.08, 0.27)	5, 0.34 (0.22, 0.46)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.CF.KM.S7.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	43 (49.4)	61 (52.1)
	Median Survival Est. (95% CI)	2.20 (1.41, 5.52)	1.05 (0.79, 1.74)
	Hazard Ratio (95% CI)		0.689 (0.466, 1.018)
	Treatment P-value [a]		0.05651
	Interaction P-value [b]		0.03084
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.36 (0.23, 0.49)	6, 0.25 (0.15, 0.36)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.20 (0.07, 0.38)	1, 0.10 (0.01, 0.31)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.CF.KM.S7.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	26 (35.6)	32 (41.0)
	Median Survival Est. (95% CI)	5.95 (1.45, NC)	1.28 (0.76, NC)
	Hazard Ratio (95% CI)		0.695 (0.414, 1.167)
	Treatment P-value [a]		0.19023
	Interaction P-value [b]		0.03084
6 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.43 (0.24, 0.61)	4, 0.41 (0.28, 0.54)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.31 (0.13, 0.51)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.CF.KM.S8.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	55 (56.1)	59 (55.1)
	Median Survival Est. (95% CI)	1.08 (0.69, 1.91)	1.15 (0.79, 1.94)
	Hazard Ratio (95% CI)		1.016 (0.703, 1.467)
	Treatment P-value [a]		0.90530
	Interaction P-value [b]		0.61171
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.22 (0.12, 0.34)	6, 0.28 (0.18, 0.40)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.CF.KM.S8.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	100 (49.3)	84 (42.0)
	Median Survival Est. (95% CI)	1.77 (1.48, 2.69)	1.48 (0.99, 2.37)
	Hazard Ratio (95% CI)		0.900 (0.673, 1.203)
	Treatment P-value [a]		0.48972
	Interaction P-value [b]		0.61171
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.31 (0.22, 0.41)	9, 0.35 (0.26, 0.44)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.21 (0.11, 0.34)	2, 0.27 (0.15, 0.39)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.CF.KM.S9.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	133 (50.8)	124 (45.9)
	Median Survival Est. (95% CI)	1.74 (1.31, 2.40)	1.45 (1.02, 1.74)
	Hazard Ratio (95% CI)		0.898 (0.703, 1.147)
	Treatment P-value [a]		0.37183
	Interaction P-value [b]		0.50562
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.28 (0.20, 0.36)	13, 0.32 (0.24, 0.39)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.20 (0.11, 0.31)	1, 0.13 (0.04, 0.28)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.CF.KM.S9.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	22 (56.4)	19 (51.4)
	Median Survival Est. (95% CI)	0.99 (0.59, 2.46)	1.25 (0.39, NC)
	Hazard Ratio (95% CI)		1.124 (0.608, 2.079)
	Treatment P-value [a]		0.78288
	Interaction P-value [b]		0.50562
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.31 (0.15, 0.49)	2, 0.35 (0.19, 0.52)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.35 (0.19, 0.52)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.CF.KM.S10.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	34 (55.7)	35 (70.0)
	Median Survival Est. (95% CI)	1.74 (1.22, 2.63)	1.02 (0.76, 1.51)
	Hazard Ratio (95% CI)		0.585 (0.365, 0.939)
	Treatment P-value [a]		0.02623
	Interaction P-value [b]		0.02382
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.25 (0.12, 0.42)	2, 0.14 (0.05, 0.28)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.CF.KM.S10.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	108 (52.2)	90 (41.9)
	Median Survival Est. (95% CI)	1.48 (0.99, 2.20)	1.48 (1.02, 2.37)
	Hazard Ratio (95% CI)		1.103 (0.833, 1.459)
	Treatment P-value [a]		0.49293
	Interaction P-value [b]		0.02382
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.27 (0.19, 0.36)	12, 0.38 (0.30, 0.47)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.17 (0.08, 0.29)	2, 0.23 (0.09, 0.40)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

3.1.1.6 Soziale Funktion

Astellas: 7465-CL-0301
Table EORTC10.SF.KM.S1.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	63 (58.3)	51 (45.9)
	Median Survival Est. (95% CI)	0.82 (0.56, 1.45)	0.99 (0.76, 1.68)
	Hazard Ratio (95% CI)		0.995 (0.687, 1.440)
	Treatment P-value [a]		0.85733
	Interaction P-value [b]		0.34577
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.25 (0.14, 0.37)	3, 0.28 (0.17, 0.39)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.SF.KM.S1.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	104 (53.9)	105 (53.6)
	Median Survival Est. (95% CI)	1.08 (0.79, 1.71)	0.85 (0.72, 1.08)
	Hazard Ratio (95% CI)		0.798 (0.608, 1.047)
	Treatment P-value [a]		0.12116
	Interaction P-value [b]		0.34577
6 Months	Patients at Risk, Survival Est. (95% CI)	14, 0.31 (0.23, 0.39)	8, 0.22 (0.14, 0.30)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.12 (0.01, 0.33)	1, 0.14 (0.05, 0.29)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.SF.KM.S2.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	143 (57.4)	118 (49.4)
	Median Survival Est. (95% CI)	0.99 (0.69, 1.41)	0.82 (0.72, 1.18)
	Hazard Ratio (95% CI)		0.868 (0.680, 1.108)
	Treatment P-value [a]		0.25345
	Interaction P-value [b]		0.83778
6 Months	Patients at Risk, Survival Est. (95% CI)	18, 0.28 (0.21, 0.36)	8, 0.24 (0.17, 0.32)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Astellas: 7465-CL-0301
Table EORTC10.SF.KM.S2.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	24 (46.2)	38 (55.9)
	Median Survival Est. (95% CI)	1.02 (0.49, 1.94)	0.99 (0.72, 1.25)
	Hazard Ratio (95% CI)		0.818 (0.490, 1.365)
	Treatment P-value [a]		0.48766
	Interaction P-value [b]		0.83778
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.34 (0.19, 0.50)	3, 0.21 (0.10, 0.35)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.34 (0.19, 0.50)	1, 0.11 (0.01, 0.32)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Table EORTC10.SF.KM.S3.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	138 (58.0)	116 (50.0)
	Median Survival Est. (95% CI)	0.99 (0.76, 1.28)	0.89 (0.72, 1.18)
	Hazard Ratio (95% CI)		0.916 (0.715, 1.173)
	Treatment P-value [a]		0.49647
	Interaction P-value [b]		0.26530
6 Months	Patients at Risk, Survival Est. (95% CI)	18, 0.27 (0.20, 0.35)	9, 0.25 (0.17, 0.33)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.08 (0.01, 0.24)	1, 0.16 (0.05, 0.33)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Astellas: 7465-CL-0301
Table EORTC10.SF.KM.S3.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	29 (46.0)	40 (53.3)
	Median Survival Est. (95% CI)	1.22 (0.53, NC)	0.99 (0.76, 1.22)
	Hazard Ratio (95% CI)		0.675 (0.418, 1.089)
	Treatment P-value [a]		0.11310
	Interaction P-value [b]		0.26530
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.36 (0.21, 0.52)	2, 0.20 (0.10, 0.33)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.SF.KM.S4.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	60 (47.6)	60 (46.5)
	Median Survival Est. (95% CI)	1.25 (0.69, 2.23)	0.72 (0.39, 1.05)
	Hazard Ratio (95% CI)		0.690 (0.482, 0.988)
	Treatment P-value [a]		0.04576
	Interaction P-value [b]		0.29901
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.30 (0.19, 0.43)	5, 0.19 (0.10, 0.30)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.SF.KM.S4.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	18 (41.9)	17 (38.6)
	Median Survival Est. (95% CI)	1.51 (0.46, NC)	1.08 (0.72, NC)
	Hazard Ratio (95% CI)		0.901 (0.463, 1.756)
	Treatment P-value [a]		0.80334
	Interaction P-value [b]		0.29901
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.38 (0.18, 0.57)	0
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.19 (0.02, 0.50)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.SF.KM.S4.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	89 (67.4)	79 (59.0)
	Median Survival Est. (95% CI)	0.89 (0.59, 1.22)	0.92 (0.76, 1.41)
	Hazard Ratio (95% CI)		1.000 (0.738, 1.355)
	Treatment P-value [a]		0.94504
	Interaction P-value [b]		0.29901
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.26 (0.17, 0.35)	6, 0.25 (0.17, 0.34)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.25 (0.17, 0.34)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.SF.KM.S5.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	77 (64.2)	64 (51.6)
	Median Survival Est. (95% CI)	0.99 (0.59, 1.45)	1.08 (0.82, 1.61)
	Hazard Ratio (95% CI)		1.090 (0.782, 1.520)
	Treatment P-value [a]		0.64690
	Interaction P-value [b]		0.05702
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.23 (0.14, 0.34)	5, 0.32 (0.23, 0.42)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.SF.KM.S5.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	90 (49.7)	92 (50.3)
	Median Survival Est. (95% CI)	1.02 (0.69, 1.74)	0.76 (0.53, 0.99)
	Hazard Ratio (95% CI)		0.710 (0.531, 0.951)
	Treatment P-value [a]		0.02502
	Interaction P-value [b]		0.05702
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.34 (0.25, 0.43)	6, 0.16 (0.09, 0.25)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.11 (0.01, 0.33)	1, 0.11 (0.03, 0.23)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.SF.KM.S6.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	47 (50.5)	45 (47.4)
	Median Survival Est. (95% CI)	0.89 (0.59, 1.74)	0.76 (0.53, 1.28)
	Hazard Ratio (95% CI)		0.772 (0.512, 1.163)
	Treatment P-value [a]		0.24065
	Interaction P-value [b]		0.54068
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.30 (0.18, 0.43)	1, 0.18 (0.09, 0.31)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.26 (0.13, 0.40)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.SF.KM.S6.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	120 (57.7)	111 (52.4)
	Median Survival Est. (95% CI)	1.02 (0.79, 1.45)	0.99 (0.76, 1.18)
	Hazard Ratio (95% CI)		0.898 (0.693, 1.163)
	Treatment P-value [a]		0.42875
	Interaction P-value [b]		0.54068
6 Months	Patients at Risk, Survival Est. (95% CI)	15, 0.29 (0.21, 0.37)	10, 0.25 (0.18, 0.33)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.17 (0.06, 0.33)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.SF.KM.S7.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	85 (60.3)	56 (50.0)
	Median Survival Est. (95% CI)	0.82 (0.59, 1.22)	1.05 (0.76, 1.61)
	Hazard Ratio (95% CI)		1.071 (0.764, 1.502)
	Treatment P-value [a]		0.68337
	Interaction P-value [b]		0.14897
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.26 (0.17, 0.36)	5, 0.24 (0.14, 0.35)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.SF.KM.S7.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	50 (57.5)	58 (49.6)
	Median Survival Est. (95% CI)	0.85 (0.53, 1.87)	0.76 (0.36, 1.08)
	Hazard Ratio (95% CI)		0.837 (0.573, 1.224)
	Treatment P-value [a]		0.45540
	Interaction P-value [b]		0.14897
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.30 (0.19, 0.42)	3, 0.27 (0.17, 0.39)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.10 (0.01, 0.32)	1, 0.27 (0.17, 0.39)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.SF.KM.S7.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	32 (43.8)	42 (53.8)
	Median Survival Est. (95% CI)	1.74 (0.95, 6.83)	0.82 (0.53, 1.51)
	Hazard Ratio (95% CI)		0.609 (0.384, 0.964)
	Treatment P-value [a]		0.02838
	Interaction P-value [b]		0.14897
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.32 (0.16, 0.50)	3, 0.19 (0.09, 0.31)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC10.SF.KM.S8.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	54 (55.1)	67 (62.6)
	Median Survival Est. (95% CI)	1.02 (0.72, 1.54)	0.76 (0.53, 0.99)
	Hazard Ratio (95% CI)		0.719 (0.502, 1.029)
	Treatment P-value [a]		0.06791
	Interaction P-value [b]		0.19738
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.29 (0.18, 0.40)	4, 0.19 (0.11, 0.29)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.SF.KM.S8.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	113 (55.7)	89 (44.5)
	Median Survival Est. (95% CI)	0.99 (0.59, 1.71)	1.05 (0.76, 1.28)
	Hazard Ratio (95% CI)		0.969 (0.733, 1.280)
	Treatment P-value [a]		0.82409
	Interaction P-value [b]		0.19738
6 Months	Patients at Risk, Survival Est. (95% CI)	14, 0.29 (0.20, 0.38)	7, 0.26 (0.18, 0.36)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.09 (0.01, 0.28)	1, 0.26 (0.18, 0.36)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC10.SF.KM.S9.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	144 (55.0)	136 (50.4)
	Median Survival Est. (95% CI)	0.99 (0.69, 1.28)	0.92 (0.76, 1.18)
	Hazard Ratio (95% CI)		0.846 (0.669, 1.071)
	Treatment P-value [a]		0.17045
	Interaction P-value [b]		0.67784
6 Months	Patients at Risk, Survival Est. (95% CI)	21, 0.30 (0.23, 0.38)	8, 0.22 (0.15, 0.29)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.10 (0.01, 0.30)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.SF.KM.S9.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	23 (59.0)	20 (54.1)
	Median Survival Est. (95% CI)	1.41 (0.69, 5.42)	0.76 (0.36, 10.87)
	Hazard Ratio (95% CI)		0.971 (0.532, 1.771)
	Treatment P-value [a]		0.97898
	Interaction P-value [b]		0.67784
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.19 (0.05, 0.41)	3, 0.35 (0.19, 0.53)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.18 (0.02, 0.48)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.SF.KM.S10.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	42 (68.9)	32 (64.0)
	Median Survival Est. (95% CI)	0.69 (0.53, 1.41)	0.76 (0.33, 1.51)
	Hazard Ratio (95% CI)		0.842 (0.531, 1.333)
	Treatment P-value [a]		0.44750
	Interaction P-value [b]		0.89989
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.20 (0.09, 0.33)	2, 0.15 (0.05, 0.29)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC10.SF.KM.S10.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 10 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	106 (51.2)	105 (48.8)
	Median Survival Est. (95% CI)	0.99 (0.69, 1.54)	0.89 (0.76, 1.18)
	Hazard Ratio (95% CI)		0.871 (0.665, 1.141)
	Treatment P-value [a]		0.31953
	Interaction P-value [b]		0.89989
6 Months	Patients at Risk, Survival Est. (95% CI)	16, 0.32 (0.24, 0.41)	8, 0.25 (0.17, 0.33)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.20 (0.11, 0.32)	1, 0.17 (0.05, 0.33)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

3.1.2 Sensitivitätsanalyse (Responderschwelle ≥ 15 Punkte)

3.1.2.1 Globaler Gesundheitsstatus

Astellas: 7465-CL-0301
Table EORTC15.QL.KM.S1.FAS: EORTC Global Health Status: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	58 (53.7)	43 (38.7)
	Median Survival Est. (95% CI)	1.45 (0.82, 2.17)	2.17 (0.99, 5.36)
	Hazard Ratio (95% CI)		1.163 (0.784, 1.726)
	Treatment P-value [a]		0.46600
	Interaction P-value [b]		0.02056
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.35 (0.24, 0.45)	5, 0.31 (0.16, 0.47)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.QL.KM.S1.FAS: EORTC Global Health Status: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	104 (53.9)	113 (57.7)
	Median Survival Est. (95% CI)	1.41 (1.02, 1.94)	0.95 (0.62, 1.12)
	Hazard Ratio (95% CI)		0.662 (0.507, 0.865)
	Treatment P-value [a]		0.00259
	Interaction P-value [b]		0.02056
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.24 (0.16, 0.33)	6, 0.17 (0.11, 0.25)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.18 (0.10, 0.29)	1, 0.12 (0.04, 0.24)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.18 (0.10, 0.29)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.QL.KM.S2.FAS: EORTC Global Health Status: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	134 (53.8)	115 (48.1)
	Median Survival Est. (95% CI)	1.51 (1.05, 2.14)	1.02 (0.79, 1.68)
	Hazard Ratio (95% CI)		0.805 (0.627, 1.033)
	Treatment P-value [a]		0.08586
	Interaction P-value [b]		0.85297
6 Months	Patients at Risk, Survival Est. (95% CI)	18, 0.28 (0.20, 0.36)	8, 0.22 (0.14, 0.32)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.18 (0.10, 0.28)	0
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.18 (0.10, 0.28)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.QL.KM.S2.FAS: EORTC Global Health Status: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	28 (53.8)	41 (60.3)
	Median Survival Est. (95% CI)	1.02 (0.56, 1.54)	0.99 (0.56, 1.22)
	Hazard Ratio (95% CI)		0.847 (0.524, 1.370)
	Treatment P-value [a]		0.49670
	Interaction P-value [b]		0.85297
6 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.20 (0.06, 0.41)	3, 0.20 (0.10, 0.32)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.20 (0.10, 0.32)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.QL.KM.S3.FAS: EORTC Global Health Status: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	130 (54.6)	115 (49.6)
	Median Survival Est. (95% CI)	1.22 (0.95, 1.81)	0.99 (0.76, 1.28)
	Hazard Ratio (95% CI)		0.833 (0.648, 1.071)
	Treatment P-value [a]		0.17759
	Interaction P-value [b]		0.47947
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.27 (0.20, 0.35)	8, 0.24 (0.16, 0.33)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.17 (0.09, 0.27)	1, 0.14 (0.04, 0.30)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.17 (0.09, 0.27)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.QL.KM.S3.FAS: EORTC Global Health Status: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	32 (50.8)	41 (54.7)
	Median Survival Est. (95% CI)	2.17 (1.02, 5.52)	0.99 (0.76, 1.77)
	Hazard Ratio (95% CI)		0.689 (0.434, 1.095)
	Treatment P-value [a]		0.07094
	Interaction P-value [b]		0.47947
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.22 (0.08, 0.41)	3, 0.15 (0.05, 0.29)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.QL.KM.S4.FAS: EORTC Global Health Status: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	55 (43.7)	56 (43.4)
	Median Survival Est. (95% CI)	1.81 (0.95, 5.36)	0.79 (0.36, 1.15)
	Hazard Ratio (95% CI)		0.658 (0.454, 0.956)
	Treatment P-value [a]		0.02969
	Interaction P-value [b]		0.31412
6 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.34 (0.21, 0.47)	5, 0.27 (0.17, 0.38)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.QL.KM.S4.FAS: EORTC Global Health Status: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	19 (44.2)	18 (40.9)
	Median Survival Est. (95% CI)	1.38 (0.53, 5.49)	2.17 (0.82, 2.69)
	Hazard Ratio (95% CI)		1.147 (0.601, 2.186)
	Treatment P-value [a]		0.57073
	Interaction P-value [b]		0.31412
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.26 (0.09, 0.47)	2, 0.27 (0.11, 0.46)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.QL.KM.S4.FAS: EORTC Global Health Status: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	88 (66.7)	82 (61.2)
	Median Survival Est. (95% CI)	1.31 (0.99, 1.87)	0.99 (0.76, 1.38)
	Hazard Ratio (95% CI)		0.834 (0.617, 1.128)
	Treatment P-value [a]		0.18119
	Interaction P-value [b]		0.31412
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.22 (0.14, 0.32)	4, 0.17 (0.08, 0.29)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.11 (0.04, 0.21)	1, 0.06 (0.01, 0.22)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.11 (0.04, 0.21)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.QL.KM.S5.FAS: EORTC Global Health Status: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	73 (60.8)	71 (57.3)
	Median Survival Est. (95% CI)	1.41 (0.99, 1.97)	1.02 (0.82, 1.68)
	Hazard Ratio (95% CI)		0.815 (0.587, 1.131)
	Treatment P-value [a]		0.18450
	Interaction P-value [b]		0.87901
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.28 (0.19, 0.39)	2, 0.19 (0.08, 0.33)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.13 (0.04, 0.27)	0
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.13 (0.04, 0.27)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.QL.KM.S5.FAS: EORTC Global Health Status: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	89 (49.2)	85 (46.4)
	Median Survival Est. (95% CI)	1.38 (0.85, 2.30)	0.99 (0.56, 1.25)
	Hazard Ratio (95% CI)		0.787 (0.585, 1.060)
	Treatment P-value [a]		0.12576
	Interaction P-value [b]		0.87901
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.25 (0.16, 0.35)	9, 0.24 (0.15, 0.33)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.20 (0.10, 0.31)	1, 0.21 (0.13, 0.31)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.QL.KM.S6.FAS: EORTC Global Health Status: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	43 (46.2)	43 (45.3)
	Median Survival Est. (95% CI)	1.74 (0.95, 6.34)	1.12 (0.56, 1.38)
	Hazard Ratio (95% CI)		0.653 (0.427, 0.998)
	Treatment P-value [a]		0.03853
	Interaction P-value [b]		0.27079
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.36 (0.22, 0.50)	1, 0.19 (0.09, 0.32)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.QL.KM.S6.FAS: EORTC Global Health Status: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	119 (57.2)	113 (53.3)
	Median Survival Est. (95% CI)	1.41 (0.99, 1.87)	0.99 (0.76, 1.41)
	Hazard Ratio (95% CI)		0.862 (0.666, 1.116)
	Treatment P-value [a]		0.28181
	Interaction P-value [b]		0.27079
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.23 (0.15, 0.32)	10, 0.24 (0.16, 0.33)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.18 (0.10, 0.28)	1, 0.16 (0.07, 0.29)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.18 (0.10, 0.28)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.QL.KM.S7.FAS: EORTC Global Health Status: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	80 (56.7)	56 (50.0)
	Median Survival Est. (95% CI)	1.25 (0.79, 2.10)	1.05 (0.53, 1.91)
	Hazard Ratio (95% CI)		0.858 (0.609, 1.207)
	Treatment P-value [a]		0.37033
	Interaction P-value [b]		0.84632
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.24 (0.14, 0.34)	5, 0.24 (0.13, 0.37)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.18 (0.09, 0.29)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.QL.KM.S7.FAS: EORTC Global Health Status: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	48 (55.2)	63 (53.8)
	Median Survival Est. (95% CI)	1.41 (0.82, 2.37)	0.99 (0.76, 1.38)
	Hazard Ratio (95% CI)		0.739 (0.507, 1.077)
	Treatment P-value [a]		0.11252
	Interaction P-value [b]		0.84632
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.29 (0.17, 0.42)	2, 0.17 (0.07, 0.30)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.16 (0.06, 0.32)	1, 0.17 (0.07, 0.30)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.16 (0.06, 0.32)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.QL.KM.S7.FAS: EORTC Global Health Status: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	34 (46.6)	37 (47.4)
	Median Survival Est. (95% CI)	1.74 (0.95, 5.95)	0.99 (0.56, 1.77)
	Hazard Ratio (95% CI)		0.790 (0.496, 1.258)
	Treatment P-value [a]		0.27775
	Interaction P-value [b]		0.84632
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.29 (0.12, 0.49)	4, 0.27 (0.15, 0.41)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.QL.KM.S8.FAS: EORTC Global Health Status: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	54 (55.1)	67 (62.6)
	Median Survival Est. (95% CI)	1.22 (0.72, 1.54)	0.79 (0.39, 0.99)
	Hazard Ratio (95% CI)		0.683 (0.477, 0.979)
	Treatment P-value [a]		0.04663
	Interaction P-value [b]		0.25278
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.30 (0.19, 0.41)	3, 0.18 (0.09, 0.28)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.08 (0.01, 0.27)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.QL.KM.S8.FAS: EORTC Global Health Status: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	108 (53.2)	89 (44.5)
	Median Survival Est. (95% CI)	1.74 (1.02, 2.14)	1.22 (0.99, 1.97)
	Hazard Ratio (95% CI)		0.891 (0.673, 1.180)
	Treatment P-value [a]		0.42164
	Interaction P-value [b]		0.25278
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.24 (0.16, 0.34)	8, 0.26 (0.17, 0.36)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.18 (0.10, 0.30)	1, 0.23 (0.13, 0.34)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.18 (0.10, 0.30)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.QL.KM.S9.FAS: EORTC Global Health Status: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	141 (53.8)	139 (51.5)
	Median Survival Est. (95% CI)	1.38 (1.02, 1.91)	0.99 (0.76, 1.18)
	Hazard Ratio (95% CI)		0.774 (0.612, 0.979)
	Treatment P-value [a]		0.02942
	Interaction P-value [b]		0.46118
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.25 (0.18, 0.33)	9, 0.20 (0.14, 0.28)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.16 (0.08, 0.26)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.QL.KM.S9.FAS: EORTC Global Health Status: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	21 (53.8)	17 (45.9)
	Median Survival Est. (95% CI)	1.71 (0.76, 6.34)	2.17 (0.33, NC)
	Hazard Ratio (95% CI)		1.000 (0.527, 1.896)
	Treatment P-value [a]		0.96675
	Interaction P-value [b]		0.46118
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.35 (0.16, 0.56)	2, 0.35 (0.15, 0.56)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.12 (0.01, 0.38)	1, 0.35 (0.15, 0.56)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.12 (0.01, 0.38)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.QL.KM.S10.FAS: EORTC Global Health Status: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	38 (62.3)	29 (58.0)
	Median Survival Est. (95% CI)	1.18 (0.59, 1.71)	0.99 (0.62, 2.46)
	Hazard Ratio (95% CI)		0.907 (0.559, 1.471)
	Treatment P-value [a]		0.62508
	Interaction P-value [b]		0.57979
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.20 (0.07, 0.39)	3, 0.20 (0.07, 0.39)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.10 (0.01, 0.32)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.QL.KM.S10.FAS: EORTC Global Health Status: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	105 (50.7)	107 (49.8)
	Median Survival Est. (95% CI)	1.45 (0.95, 2.10)	1.02 (0.66, 1.25)
	Hazard Ratio (95% CI)		0.775 (0.592, 1.016)
	Treatment P-value [a]		0.07244
	Interaction P-value [b]		0.57979
6 Months	Patients at Risk, Survival Est. (95% CI)	14, 0.31 (0.22, 0.39)	6, 0.23 (0.15, 0.31)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.20 (0.11, 0.31)	1, 0.23 (0.15, 0.31)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.20 (0.11, 0.31)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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3.1.2.2 Körperliche Funktion

Astellas: 7465-CL-0301
Table EORTC15.PF.KM.S1.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	42 (38.9)	37 (33.3)
	Median Survival Est. (95% CI)	6.21 (4.67, 7.16)	4.99 (2.40, 7.69)
	Hazard Ratio (95% CI)		0.974 (0.626, 1.516)
	Treatment P-value [a]		0.83751
	Interaction P-value [b]		0.18944
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.52 (0.37, 0.65)	8, 0.43 (0.28, 0.58)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.PF.KM.S1.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	76 (39.4)	83 (42.3)
	Median Survival Est. (95% CI)	6.34 (2.23, 12.25)	1.71 (1.22, 2.79)
	Hazard Ratio (95% CI)		0.678 (0.494, 0.929)
	Treatment P-value [a]		0.03776
	Interaction P-value [b]		0.18944
6 Months	Patients at Risk, Survival Est. (95% CI)	24, 0.51 (0.42, 0.59)	10, 0.34 (0.23, 0.44)
12 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.40 (0.29, 0.52)	2, 0.25 (0.13, 0.39)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.15 (0.01, 0.43)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.PF.KM.S2.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	97 (39.0)	90 (37.7)
	Median Survival Est. (95% CI)	6.34 (5.16, 7.56)	2.66 (1.94, 5.42)
	Hazard Ratio (95% CI)		0.756 (0.567, 1.010)
	Treatment P-value [a]		0.03947
	Interaction P-value [b]		0.57105
6 Months	Patients at Risk, Survival Est. (95% CI)	32, 0.53 (0.44, 0.61)	14, 0.38 (0.27, 0.48)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.29 (0.18, 0.41)	0
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.19 (0.06, 0.38)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.PF.KM.S2.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	21 (40.4)	30 (44.1)
	Median Survival Est. (95% CI)	2.07 (0.56, NC)	1.54 (1.02, 4.14)
	Hazard Ratio (95% CI)		0.907 (0.518, 1.591)
	Treatment P-value [a]		0.90637
	Interaction P-value [b]		0.57105
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.45 (0.29, 0.61)	4, 0.35 (0.21, 0.49)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.45 (0.29, 0.61)	2, 0.35 (0.21, 0.49)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.PF.KM.S3.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	101 (42.4)	93 (40.1)
	Median Survival Est. (95% CI)	5.68 (2.10, 6.83)	2.37 (1.61, 4.99)
	Hazard Ratio (95% CI)		0.801 (0.603, 1.065)
	Treatment P-value [a]		0.12937
	Interaction P-value [b]		0.39536
6 Months	Patients at Risk, Survival Est. (95% CI)	30, 0.49 (0.41, 0.57)	13, 0.36 (0.26, 0.46)
12 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.30 (0.20, 0.41)	1, 0.16 (0.06, 0.29)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.11 (0.01, 0.34)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.PF.KM.S3.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	17 (27.0)	27 (36.0)
	Median Survival Est. (95% CI)	8.18 (5.52, NC)	2.46 (1.54, NC)
	Hazard Ratio (95% CI)		0.599 (0.326, 1.100)
	Treatment P-value [a]		0.08093
	Interaction P-value [b]		0.39536
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.61 (0.41, 0.77)	5, 0.40 (0.22, 0.56)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.40 (0.22, 0.56)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.PF.KM.S4.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	42 (33.3)	39 (30.2)
	Median Survival Est. (95% CI)	5.68 (4.67, 8.08)	2.00 (1.02, NC)
	Hazard Ratio (95% CI)		0.813 (0.526, 1.259)
	Treatment P-value [a]		0.40473
	Interaction P-value [b]		0.92018
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.48 (0.33, 0.62)	7, 0.47 (0.35, 0.58)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.47 (0.35, 0.58)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.PF.KM.S4.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	12 (27.9)	12 (27.3)
	Median Survival Est. (95% CI)	16.56 (1.71, NC)	4.99 (1.94, NC)
	Hazard Ratio (95% CI)		0.824 (0.368, 1.843)
	Treatment P-value [a]		0.76349
	Interaction P-value [b]		0.92018
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.59 (0.38, 0.75)	2, 0.41 (0.15, 0.66)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.59 (0.38, 0.75)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.PF.KM.S4.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	64 (48.5)	69 (51.5)
	Median Survival Est. (95% CI)	6.34 (1.71, 8.11)	2.37 (1.68, 5.36)
	Hazard Ratio (95% CI)		0.733 (0.520, 1.035)
	Treatment P-value [a]		0.05562
	Interaction P-value [b]		0.92018
6 Months	Patients at Risk, Survival Est. (95% CI)	22, 0.51 (0.41, 0.60)	9, 0.31 (0.19, 0.43)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.26 (0.14, 0.41)	1, 0.05 (0.00, 0.19)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.18 (0.05, 0.37)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.PF.KM.S5.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	47 (39.2)	50 (40.3)
	Median Survival Est. (95% CI)	6.54 (5.52, NC)	4.37 (1.94, 7.69)
	Hazard Ratio (95% CI)		0.724 (0.484, 1.083)
	Treatment P-value [a]		0.08450
	Interaction P-value [b]		0.69366
6 Months	Patients at Risk, Survival Est. (95% CI)	20, 0.56 (0.43, 0.66)	8, 0.42 (0.28, 0.55)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.41 (0.26, 0.54)	1, 0.15 (0.03, 0.35)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.20 (0.02, 0.52)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.PF.KM.S5.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	71 (39.2)	70 (38.3)
	Median Survival Est. (95% CI)	5.16 (2.07, 7.16)	1.84 (1.18, 2.79)
	Hazard Ratio (95% CI)		0.803 (0.577, 1.119)
	Treatment P-value [a]		0.21758
	Interaction P-value [b]		0.69366
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.49 (0.39, 0.58)	10, 0.33 (0.22, 0.44)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.25 (0.13, 0.40)	1, 0.25 (0.13, 0.39)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.PF.KM.S6.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	34 (36.6)	38 (40.0)
	Median Survival Est. (95% CI)	6.47 (2.17, NC)	1.28 (0.99, 2.37)
	Hazard Ratio (95% CI)		0.598 (0.375, 0.954)
	Treatment P-value [a]		0.04517
	Interaction P-value [b]		0.22186
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.52 (0.38, 0.65)	2, 0.33 (0.21, 0.46)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.33 (0.16, 0.50)	1, 0.33 (0.21, 0.46)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.PF.KM.S6.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	84 (40.4)	82 (38.7)
	Median Survival Est. (95% CI)	6.21 (3.58, 8.08)	4.14 (2.14, 5.49)
	Hazard Ratio (95% CI)		0.846 (0.623, 1.149)
	Treatment P-value [a]		0.27731
	Interaction P-value [b]		0.22186
6 Months	Patients at Risk, Survival Est. (95% CI)	24, 0.52 (0.42, 0.60)	16, 0.40 (0.29, 0.50)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.32 (0.19, 0.44)	1, 0.21 (0.10, 0.34)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.21 (0.06, 0.42)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.PF.KM.S7.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	64 (45.4)	42 (37.5)
	Median Survival Est. (95% CI)	5.16 (1.61, 7.56)	2.66 (1.54, 5.49)
	Hazard Ratio (95% CI)		0.916 (0.619, 1.355)
	Treatment P-value [a]		0.60836
	Interaction P-value [b]		0.18389
6 Months	Patients at Risk, Survival Est. (95% CI)	19, 0.47 (0.37, 0.57)	4, 0.30 (0.14, 0.48)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.20 (0.08, 0.36)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.PF.KM.S7.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	29 (33.3)	51 (43.6)
	Median Survival Est. (95% CI)	16.56 (2.40, NC)	2.40 (1.84, 5.42)
	Hazard Ratio (95% CI)		0.530 (0.332, 0.846)
	Treatment P-value [a]		0.00634
	Interaction P-value [b]		0.18389
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.62 (0.49, 0.72)	8, 0.34 (0.20, 0.47)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.52 (0.34, 0.66)	1, 0.06 (0.00, 0.23)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.26 (0.02, 0.62)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.PF.KM.S7.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	25 (34.2)	27 (34.6)
	Median Survival Est. (95% CI)	5.52 (1.91, NC)	1.71 (0.99, NC)
	Hazard Ratio (95% CI)		0.863 (0.501, 1.488)
	Treatment P-value [a]		0.57346
	Interaction P-value [b]		0.18389
6 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.46 (0.26, 0.64)	6, 0.48 (0.34, 0.61)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.48 (0.34, 0.61)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.PF.KM.S8.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	40 (40.8)	50 (46.7)
	Median Survival Est. (95% CI)	6.34 (1.64, 7.56)	1.94 (1.22, 5.36)
	Hazard Ratio (95% CI)		0.746 (0.491, 1.133)
	Treatment P-value [a]		0.12888
	Interaction P-value [b]		0.81330
6 Months	Patients at Risk, Survival Est. (95% CI)	14, 0.54 (0.42, 0.65)	5, 0.35 (0.21, 0.48)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.21 (0.07, 0.40)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.PF.KM.S8.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	78 (38.4)	70 (35.0)
	Median Survival Est. (95% CI)	5.68 (3.58, 8.38)	2.66 (1.84, 6.70)
	Hazard Ratio (95% CI)		0.795 (0.574, 1.101)
	Treatment P-value [a]		0.18139
	Interaction P-value [b]		0.81330
6 Months	Patients at Risk, Survival Est. (95% CI)	23, 0.50 (0.40, 0.59)	13, 0.39 (0.28, 0.50)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.37 (0.25, 0.49)	2, 0.24 (0.12, 0.38)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.18 (0.02, 0.48)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.PF.KM.S9.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	100 (38.2)	108 (40.0)
	Median Survival Est. (95% CI)	6.34 (4.67, 8.08)	2.37 (1.61, 4.99)
	Hazard Ratio (95% CI)		0.703 (0.534, 0.925)
	Treatment P-value [a]		0.00890
	Interaction P-value [b]		0.07943
6 Months	Patients at Risk, Survival Est. (95% CI)	34, 0.52 (0.44, 0.60)	15, 0.35 (0.26, 0.44)
12 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.32 (0.22, 0.43)	1, 0.17 (0.08, 0.30)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.PF.KM.S9.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	18 (46.2)	12 (32.4)
	Median Survival Est. (95% CI)	2.63 (0.79, NC)	NC (2.00, NC)
	Hazard Ratio (95% CI)		1.426 (0.679, 2.995)
	Treatment P-value [a]		0.32646
	Interaction P-value [b]		0.07943
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.49 (0.30, 0.65)	3, 0.51 (0.27, 0.70)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.24 (0.02, 0.60)	1, 0.51 (0.27, 0.70)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.24 (0.02, 0.60)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.PF.KM.S10.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	25 (41.0)	26 (52.0)
	Median Survival Est. (95% CI)	7.16 (1.61, NC)	1.84 (0.99, 4.99)
	Hazard Ratio (95% CI)		0.613 (0.354, 1.062)
	Treatment P-value [a]		0.10085
	Interaction P-value [b]		0.28907
6 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.53 (0.38, 0.66)	4, 0.30 (0.15, 0.47)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.44 (0.24, 0.62)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.PF.KM.S10.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	81 (39.1)	78 (36.3)
	Median Survival Est. (95% CI)	6.21 (2.63, 7.56)	3.88 (1.94, 6.01)
	Hazard Ratio (95% CI)		0.863 (0.630, 1.182)
	Treatment P-value [a]		0.34465
	Interaction P-value [b]		0.28907
6 Months	Patients at Risk, Survival Est. (95% CI)	27, 0.51 (0.41, 0.59)	13, 0.41 (0.31, 0.51)
12 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.30 (0.19, 0.42)	2, 0.22 (0.10, 0.37)
18 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.15 (0.02, 0.41)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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3.1.2.3 Rollenfunktion

Astellas: 7465-CL-0301
Table EORTC15.RF.KM.S1.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	61 (56.5)	57 (51.4)
	Median Survival Est. (95% CI)	1.05 (0.79, 2.14)	1.05 (0.72, 1.71)
	Hazard Ratio (95% CI)		0.845 (0.589, 1.213)
	Treatment P-value [a]		0.36270
	Interaction P-value [b]		0.54084
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.28 (0.17, 0.40)	5, 0.20 (0.10, 0.31)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.RF.KM.S1.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	113 (58.5)	118 (60.2)
	Median Survival Est. (95% CI)	0.92 (0.72, 1.38)	0.76 (0.53, 0.95)
	Hazard Ratio (95% CI)		0.736 (0.568, 0.953)
	Treatment P-value [a]		0.02203
	Interaction P-value [b]		0.54084
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.21 (0.14, 0.30)	7, 0.14 (0.08, 0.21)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Astellas: 7465-CL-0301
Table EORTC15.RF.KM.S2.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	139 (55.8)	132 (55.2)
	Median Survival Est. (95% CI)	1.25 (0.89, 1.91)	0.79 (0.69, 1.02)
	Hazard Ratio (95% CI)		0.707 (0.557, 0.898)
	Treatment P-value [a]		0.00468
	Interaction P-value [b]		0.01491
6 Months	Patients at Risk, Survival Est. (95% CI)	19, 0.27 (0.19, 0.35)	10, 0.17 (0.11, 0.25)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Astellas: 7465-CL-0301
Table EORTC15.RF.KM.S2.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	35 (67.3)	43 (63.2)
	Median Survival Est. (95% CI)	0.56 (0.33, 0.79)	0.76 (0.53, 1.15)
	Hazard Ratio (95% CI)		1.328 (0.849, 2.075)
	Treatment P-value [a]		0.21193
	Interaction P-value [b]		0.01491
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.09 (0.02, 0.22)	2, 0.12 (0.04, 0.24)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.RF.KM.S3.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	140 (58.8)	127 (54.7)
	Median Survival Est. (95% CI)	0.99 (0.76, 1.38)	0.76 (0.62, 1.15)
	Hazard Ratio (95% CI)		0.855 (0.672, 1.087)
	Treatment P-value [a]		0.22704
	Interaction P-value [b]		0.08603
6 Months	Patients at Risk, Survival Est. (95% CI)	15, 0.23 (0.16, 0.31)	10, 0.19 (0.13, 0.27)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.RF.KM.S3.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	34 (54.0)	48 (64.0)
	Median Survival Est. (95% CI)	1.03 (0.56, 5.52)	0.82 (0.56, 1.02)
	Hazard Ratio (95% CI)		0.551 (0.354, 0.856)
	Treatment P-value [a]		0.00551
	Interaction P-value [b]		0.08603
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.27 (0.12, 0.43)	2, 0.05 (0.01, 0.15)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.RF.KM.S4.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	64 (50.8)	61 (47.3)
	Median Survival Est. (95% CI)	1.05 (0.72, 1.91)	0.72 (0.36, 0.99)
	Hazard Ratio (95% CI)		0.719 (0.506, 1.021)
	Treatment P-value [a]		0.08969
	Interaction P-value [b]		0.84350
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.25 (0.14, 0.37)	5, 0.20 (0.12, 0.30)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.RF.KM.S4.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	23 (53.5)	24 (54.5)
	Median Survival Est. (95% CI)	0.85 (0.53, 2.96)	0.82 (0.56, 1.12)
	Hazard Ratio (95% CI)		0.745 (0.420, 1.323)
	Treatment P-value [a]		0.24421
	Interaction P-value [b]		0.84350
6 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.18 (0.05, 0.37)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.RF.KM.S4.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	87 (65.9)	90 (67.2)
	Median Survival Est. (95% CI)	0.92 (0.76, 1.54)	0.82 (0.69, 1.22)
	Hazard Ratio (95% CI)		0.821 (0.611, 1.103)
	Treatment P-value [a]		0.18873
	Interaction P-value [b]		0.84350
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.24 (0.16, 0.34)	7, 0.16 (0.09, 0.26)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.RF.KM.S5.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	72 (60.0)	81 (65.3)
	Median Survival Est. (95% CI)	1.28 (0.85, 2.14)	0.82 (0.69, 1.22)
	Hazard Ratio (95% CI)		0.673 (0.489, 0.925)
	Treatment P-value [a]		0.00910
	Interaction P-value [b]		0.25085
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.28 (0.19, 0.39)	5, 0.15 (0.08, 0.25)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.RF.KM.S5.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	102 (56.4)	94 (51.4)
	Median Survival Est. (95% CI)	0.82 (0.59, 1.25)	0.76 (0.53, 0.99)
	Hazard Ratio (95% CI)		0.862 (0.652, 1.142)
	Treatment P-value [a]		0.32260
	Interaction P-value [b]		0.25085
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.20 (0.11, 0.30)	7, 0.16 (0.09, 0.25)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.RF.KM.S6.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	51 (54.8)	51 (53.7)
	Median Survival Est. (95% CI)	0.92 (0.72, 1.45)	0.59 (0.36, 0.95)
	Hazard Ratio (95% CI)		0.614 (0.415, 0.907)
	Treatment P-value [a]		0.01864
	Interaction P-value [b]		0.20116
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.22 (0.11, 0.34)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Table EORTC15.RF.KM.S6.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	123 (59.1)	124 (58.5)
	Median Survival Est. (95% CI)	1.02 (0.76, 1.54)	0.82 (0.72, 1.18)
	Hazard Ratio (95% CI)		0.831 (0.647, 1.066)
	Treatment P-value [a]		0.15828
	Interaction P-value [b]		0.20116
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.24 (0.16, 0.33)	12, 0.18 (0.12, 0.26)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Table EORTC15.RF.KM.S7.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	85 (60.3)	63 (56.3)
	Median Survival Est. (95% CI)	0.92 (0.62, 1.38)	0.82 (0.72, 1.45)
	Hazard Ratio (95% CI)		0.849 (0.612, 1.177)
	Treatment P-value [a]		0.35202
	Interaction P-value [b]		0.58316
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.25 (0.16, 0.35)	3, 0.16 (0.08, 0.26)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.RF.KM.S7.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	49 (56.3)	72 (61.5)
	Median Survival Est. (95% CI)	0.89 (0.62, 1.87)	0.76 (0.43, 1.02)
	Hazard Ratio (95% CI)		0.664 (0.462, 0.955)
	Treatment P-value [a]		0.02967
	Interaction P-value [b]		0.58316
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.24 (0.13, 0.37)	5, 0.12 (0.05, 0.22)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.RF.KM.S7.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	40 (54.8)	40 (51.3)
	Median Survival Est. (95% CI)	1.28 (0.79, 2.79)	0.79 (0.53, 1.38)
	Hazard Ratio (95% CI)		0.827 (0.533, 1.282)
	Treatment P-value [a]		0.42127
	Interaction P-value [b]		0.58316
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.22 (0.10, 0.37)	4, 0.24 (0.13, 0.36)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.RF.KM.S8.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	54 (55.1)	75 (70.1)
	Median Survival Est. (95% CI)	0.92 (0.59, 1.45)	0.72 (0.53, 0.99)
	Hazard Ratio (95% CI)		0.654 (0.460, 0.929)
	Treatment P-value [a]		0.01890
	Interaction P-value [b]		0.22321
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.31 (0.20, 0.43)	4, 0.11 (0.04, 0.20)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Astellas: 7465-CL-0301
Table EORTC15.RF.KM.S8.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	120 (59.1)	100 (50.0)
	Median Survival Est. (95% CI)	1.02 (0.76, 1.45)	0.95 (0.72, 1.22)
	Hazard Ratio (95% CI)		0.859 (0.659, 1.121)
	Treatment P-value [a]		0.27543
	Interaction P-value [b]		0.22321
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.20 (0.13, 0.29)	8, 0.19 (0.12, 0.28)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Table EORTC15.RF.KM.S9.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	150 (57.3)	152 (56.3)
	Median Survival Est. (95% CI)	0.99 (0.76, 1.38)	0.76 (0.59, 0.99)
	Hazard Ratio (95% CI)		0.744 (0.594, 0.933)
	Treatment P-value [a]		0.01189
	Interaction P-value [b]		0.40581
6 Months	Patients at Risk, Survival Est. (95% CI)	19, 0.25 (0.18, 0.32)	10, 0.16 (0.11, 0.23)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.RF.KM.S9.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	24 (61.5)	23 (62.2)
	Median Survival Est. (95% CI)	1.08 (0.49, 5.36)	0.95 (0.76, 2.56)
	Hazard Ratio (95% CI)		0.966 (0.545, 1.713)
	Treatment P-value [a]		0.76684
	Interaction P-value [b]		0.40581
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.16 (0.03, 0.37)	2, 0.15 (0.03, 0.34)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.RF.KM.S10.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	38 (62.3)	33 (66.0)
	Median Survival Est. (95% CI)	1.18 (0.56, 2.14)	0.97 (0.39, 1.51)
	Hazard Ratio (95% CI)		0.834 (0.522, 1.331)
	Treatment P-value [a]		0.47731
	Interaction P-value [b]		0.62344
6 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.16 (0.04, 0.35)	5, 0.23 (0.11, 0.38)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.RF.KM.S10.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	111 (53.6)	119 (55.3)
	Median Survival Est. (95% CI)	0.99 (0.76, 1.45)	0.76 (0.66, 1.02)
	Hazard Ratio (95% CI)		0.729 (0.562, 0.946)
	Treatment P-value [a]		0.01770
	Interaction P-value [b]		0.62344
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.29 (0.21, 0.38)	7, 0.14 (0.08, 0.22)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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3.1.2.4 Emotionale Funktion

Astellas: 7465-CL-0301
Table EORTC15.EF.KM.S1.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	45 (41.7)	40 (36.0)
	Median Survival Est. (95% CI)	3.75 (1.48, 7.56)	2.83 (2.17, 7.69)
	Hazard Ratio (95% CI)		1.039 (0.678, 1.591)
	Treatment P-value [a]		0.83599
	Interaction P-value [b]		0.08045
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.45 (0.32, 0.58)	10, 0.37 (0.23, 0.50)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.EF.KM.S1.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	71 (36.8)	84 (42.9)
	Median Survival Est. (95% CI)	5.45 (2.20, NC)	1.61 (1.05, 4.17)
	Hazard Ratio (95% CI)		0.647 (0.471, 0.888)
	Treatment P-value [a]		0.00816
	Interaction P-value [b]		0.08045
6 Months	Patients at Risk, Survival Est. (95% CI)	18, 0.41 (0.30, 0.51)	11, 0.36 (0.27, 0.46)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.20 (0.02, 0.52)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.EF.KM.S2.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	100 (40.2)	91 (38.1)
	Median Survival Est. (95% CI)	5.42 (2.43, 6.54)	2.63 (1.68, 5.32)
	Hazard Ratio (95% CI)		0.819 (0.616, 1.088)
	Treatment P-value [a]		0.17604
	Interaction P-value [b]		0.40837
6 Months	Patients at Risk, Survival Est. (95% CI)	26, 0.42 (0.32, 0.50)	18, 0.40 (0.31, 0.48)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.16 (0.02, 0.43)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.EF.KM.S2.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	16 (30.8)	33 (48.5)
	Median Survival Est. (95% CI)	5.52 (0.76, NC)	1.28 (0.99, 2.69)
	Hazard Ratio (95% CI)		0.619 (0.340, 1.126)
	Treatment P-value [a]		0.14528
	Interaction P-value [b]		0.40837
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.47 (0.22, 0.68)	3, 0.27 (0.13, 0.43)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.EF.KM.S3.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	91 (38.2)	96 (41.4)
	Median Survival Est. (95% CI)	5.42 (2.43, 7.16)	2.37 (1.45, 4.34)
	Hazard Ratio (95% CI)		0.750 (0.563, 0.999)
	Treatment P-value [a]		0.04956
	Interaction P-value [b]		0.75254
6 Months	Patients at Risk, Survival Est. (95% CI)	23, 0.44 (0.34, 0.53)	16, 0.35 (0.26, 0.44)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.17 (0.02, 0.45)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Table EORTC15.EF.KM.S3.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	25 (39.7)	28 (37.3)
	Median Survival Est. (95% CI)	5.52 (1.48, NC)	2.43 (1.08, NC)
	Hazard Ratio (95% CI)		0.827 (0.482, 1.420)
	Treatment P-value [a]		0.54745
	Interaction P-value [b]		0.75254
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.38 (0.21, 0.56)	5, 0.40 (0.25, 0.54)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.EF.KM.S4.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	39 (31.0)	47 (36.4)
	Median Survival Est. (95% CI)	5.52 (2.66, NC)	1.97 (1.08, 2.63)
	Hazard Ratio (95% CI)		0.616 (0.403, 0.942)
	Treatment P-value [a]		0.02480
	Interaction P-value [b]		0.45136
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.45 (0.30, 0.59)	7, 0.34 (0.23, 0.46)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.EF.KM.S4.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	12 (27.9)	13 (29.5)
	Median Survival Est. (95% CI)	5.45 (1.45, NC)	2.69 (0.85, NC)
	Hazard Ratio (95% CI)		0.874 (0.399, 1.917)
	Treatment P-value [a]		0.82402
	Interaction P-value [b]		0.45136
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.49 (0.24, 0.70)	3, 0.43 (0.21, 0.63)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.EF.KM.S4.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	65 (49.2)	64 (47.8)
	Median Survival Est. (95% CI)	2.63 (1.64, 5.95)	2.83 (1.22, 5.39)
	Hazard Ratio (95% CI)		0.865 (0.612, 1.222)
	Treatment P-value [a]		0.35984
	Interaction P-value [b]		0.45136
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.39 (0.28, 0.49)	11, 0.37 (0.26, 0.48)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.26 (0.13, 0.40)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.EF.KM.S5.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	50 (41.7)	49 (39.5)
	Median Survival Est. (95% CI)	5.52 (1.87, NC)	4.86 (1.97, NC)
	Hazard Ratio (95% CI)		0.892 (0.601, 1.323)
	Treatment P-value [a]		0.55202
	Interaction P-value [b]		0.30930
6 Months	Patients at Risk, Survival Est. (95% CI)	16, 0.45 (0.33, 0.57)	11, 0.46 (0.34, 0.58)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.39 (0.26, 0.52)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.EF.KM.S5.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	66 (36.5)	75 (41.0)
	Median Survival Est. (95% CI)	5.42 (2.14, 7.16)	1.48 (1.05, 2.63)
	Hazard Ratio (95% CI)		0.683 (0.490, 0.951)
	Treatment P-value [a]		0.02236
	Interaction P-value [b]		0.30930
6 Months	Patients at Risk, Survival Est. (95% CI)	14, 0.40 (0.28, 0.51)	10, 0.28 (0.19, 0.39)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.EF.KM.S6.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	31 (33.3)	37 (38.9)
	Median Survival Est. (95% CI)	5.49 (2.20, NC)	1.28 (0.85, 2.63)
	Hazard Ratio (95% CI)		0.559 (0.346, 0.902)
	Treatment P-value [a]		0.01411
	Interaction P-value [b]		0.13473
6 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.41 (0.25, 0.57)	1, 0.28 (0.14, 0.43)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.EF.KM.S6.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	85 (40.9)	87 (41.0)
	Median Survival Est. (95% CI)	5.45 (1.94, 7.56)	2.83 (1.68, 5.39)
	Hazard Ratio (95% CI)		0.860 (0.638, 1.160)
	Treatment P-value [a]		0.32669
	Interaction P-value [b]		0.13473
6 Months	Patients at Risk, Survival Est. (95% CI)	21, 0.43 (0.33, 0.52)	20, 0.39 (0.30, 0.49)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.17 (0.02, 0.45)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.EF.KM.S7.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	56 (39.7)	38 (33.9)
	Median Survival Est. (95% CI)	5.39 (2.43, 7.56)	4.17 (1.68, 8.77)
	Hazard Ratio (95% CI)		0.951 (0.630, 1.437)
	Treatment P-value [a]		0.81338
	Interaction P-value [b]		0.34611
6 Months	Patients at Risk, Survival Est. (95% CI)	15, 0.41 (0.29, 0.53)	7, 0.47 (0.34, 0.59)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.30 (0.16, 0.45)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.EF.KM.S7.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	38 (43.7)	53 (45.3)
	Median Survival Est. (95% CI)	1.94 (1.48, NC)	1.94 (0.95, 5.32)
	Hazard Ratio (95% CI)		0.785 (0.517, 1.191)
	Treatment P-value [a]		0.24075
	Interaction P-value [b]		0.34611
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.40 (0.26, 0.54)	9, 0.30 (0.18, 0.43)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.EF.KM.S7.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	22 (30.1)	33 (42.3)
	Median Survival Est. (95% CI)	5.95 (2.14, NC)	1.97 (0.99, 4.34)
	Hazard Ratio (95% CI)		0.574 (0.335, 0.986)
	Treatment P-value [a]		0.05146
	Interaction P-value [b]		0.34611
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.47 (0.26, 0.65)	5, 0.33 (0.20, 0.47)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.EF.KM.S8.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	41 (41.8)	48 (44.9)
	Median Survival Est. (95% CI)	5.42 (1.41, 7.16)	2.46 (0.99, 8.77)
	Hazard Ratio (95% CI)		0.892 (0.588, 1.355)
	Treatment P-value [a]		0.62359
	Interaction P-value [b]		0.40300
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.44 (0.30, 0.56)	10, 0.39 (0.27, 0.51)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.EF.KM.S8.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	75 (36.9)	76 (38.0)
	Median Survival Est. (95% CI)	5.45 (2.63, 8.38)	2.37 (1.45, 4.17)
	Hazard Ratio (95% CI)		0.713 (0.518, 0.981)
	Treatment P-value [a]		0.04006
	Interaction P-value [b]		0.40300
6 Months	Patients at Risk, Survival Est. (95% CI)	19, 0.41 (0.30, 0.51)	11, 0.35 (0.25, 0.45)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.19 (0.02, 0.49)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.EF.KM.S9.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	101 (38.5)	106 (39.3)
	Median Survival Est. (95% CI)	5.45 (2.20, 7.16)	2.37 (1.48, 4.34)
	Hazard Ratio (95% CI)		0.784 (0.597, 1.030)
	Treatment P-value [a]		0.08319
	Interaction P-value [b]		0.67932
6 Months	Patients at Risk, Survival Est. (95% CI)	28, 0.42 (0.33, 0.51)	20, 0.38 (0.30, 0.46)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.18 (0.02, 0.47)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.EF.KM.S9.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	15 (38.5)	18 (48.6)
	Median Survival Est. (95% CI)	5.42 (1.64, NC)	2.43 (0.95, NC)
	Hazard Ratio (95% CI)		0.671 (0.338, 1.333)
	Treatment P-value [a]		0.21102
	Interaction P-value [b]		0.67932
6 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.43 (0.20, 0.64)	1, 0.19 (0.02, 0.50)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.EF.KM.S10.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	33 (54.1)	25 (50.0)
	Median Survival Est. (95% CI)	1.91 (1.22, 5.45)	2.17 (0.99, NC)
	Hazard Ratio (95% CI)		1.016 (0.604, 1.708)
	Treatment P-value [a]		0.86911
	Interaction P-value [b]		0.22083
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.27 (0.12, 0.44)	5, 0.40 (0.24, 0.55)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.EF.KM.S10.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	69 (33.3)	82 (38.1)
	Median Survival Est. (95% CI)	5.52 (3.32, NC)	2.63 (1.38, 4.34)
	Hazard Ratio (95% CI)		0.693 (0.503, 0.956)
	Treatment P-value [a]		0.02883
	Interaction P-value [b]		0.22083
6 Months	Patients at Risk, Survival Est. (95% CI)	23, 0.48 (0.37, 0.57)	15, 0.37 (0.28, 0.47)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.41 (0.29, 0.53)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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3.1.2.5 Kognitive Funktion

Astellas: 7465-CL-0301
Table EORTC15.CF.KM.S1.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	53 (49.1)	47 (42.3)
	Median Survival Est. (95% CI)	2.07 (0.99, 5.36)	1.61 (1.02, 4.37)
	Hazard Ratio (95% CI)		1.008 (0.680, 1.493)
	Treatment P-value [a]		0.94994
	Interaction P-value [b]		0.58481
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.34 (0.22, 0.47)	6, 0.34 (0.22, 0.46)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Astellas: 7465-CL-0301
Table EORTC15.CF.KM.S1.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	102 (52.8)	96 (49.0)
	Median Survival Est. (95% CI)	1.68 (1.08, 1.94)	1.22 (0.79, 1.54)
	Hazard Ratio (95% CI)		0.881 (0.667, 1.164)
	Treatment P-value [a]		0.39122
	Interaction P-value [b]		0.58481
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.25 (0.16, 0.34)	9, 0.32 (0.24, 0.40)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.25 (0.16, 0.34)	2, 0.17 (0.07, 0.32)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.CF.KM.S2.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	130 (52.2)	113 (47.3)
	Median Survival Est. (95% CI)	1.71 (1.22, 2.20)	1.31 (0.95, 1.68)
	Hazard Ratio (95% CI)		0.871 (0.677, 1.121)
	Treatment P-value [a]		0.28612
	Interaction P-value [b]		0.37313
6 Months	Patients at Risk, Survival Est. (95% CI)	14, 0.29 (0.21, 0.37)	11, 0.31 (0.23, 0.39)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.CF.KM.S2.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	25 (48.1)	30 (44.1)
	Median Survival Est. (95% CI)	1.51 (0.56, 5.32)	1.51 (1.05, NC)
	Hazard Ratio (95% CI)		1.138 (0.669, 1.935)
	Treatment P-value [a]		0.60411
	Interaction P-value [b]		0.37313
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.25 (0.10, 0.43)	4, 0.37 (0.23, 0.51)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.25 (0.10, 0.43)	2, 0.37 (0.23, 0.51)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.CF.KM.S3.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	120 (50.4)	111 (47.8)
	Median Survival Est. (95% CI)	1.68 (1.02, 2.14)	1.45 (0.82, 1.68)
	Hazard Ratio (95% CI)		0.865 (0.668, 1.119)
	Treatment P-value [a]		0.27309
	Interaction P-value [b]		0.31762
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.32 (0.24, 0.40)	11, 0.30 (0.22, 0.39)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.21 (0.11, 0.33)	1, 0.12 (0.03, 0.26)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.CF.KM.S3.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	35 (55.6)	32 (42.7)
	Median Survival Est. (95% CI)	1.97 (1.02, 3.58)	1.45 (1.02, NC)
	Hazard Ratio (95% CI)		1.142 (0.706, 1.844)
	Treatment P-value [a]		0.69947
	Interaction P-value [b]		0.31762
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.11 (0.01, 0.33)	4, 0.38 (0.25, 0.51)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.38 (0.25, 0.51)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.CF.KM.S4.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	53 (42.1)	48 (37.2)
	Median Survival Est. (95% CI)	1.77 (0.99, 5.49)	1.08 (0.76, 6.51)
	Hazard Ratio (95% CI)		0.897 (0.607, 1.326)
	Treatment P-value [a]		0.62390
	Interaction P-value [b]		0.83428
6 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.35 (0.21, 0.49)	6, 0.40 (0.29, 0.51)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.27 (0.12, 0.44)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.CF.KM.S4.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	14 (32.6)	15 (34.1)
	Median Survival Est. (95% CI)	2.63 (1.51, NC)	1.94 (0.79, NC)
	Hazard Ratio (95% CI)		0.780 (0.376, 1.617)
	Treatment P-value [a]		0.58571
	Interaction P-value [b]		0.83428
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.42 (0.22, 0.61)	2, 0.40 (0.21, 0.59)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.42 (0.22, 0.61)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.CF.KM.S4.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	88 (66.7)	80 (59.7)
	Median Survival Est. (95% CI)	1.28 (0.95, 1.91)	1.28 (0.95, 1.64)
	Hazard Ratio (95% CI)		0.978 (0.723, 1.324)
	Treatment P-value [a]		0.87063
	Interaction P-value [b]		0.83428
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.21 (0.12, 0.31)	7, 0.26 (0.17, 0.36)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.08 (0.01, 0.26)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.CF.KM.S5.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	66 (55.0)	62 (50.0)
	Median Survival Est. (95% CI)	1.77 (1.08, 5.32)	1.61 (1.22, 3.78)
	Hazard Ratio (95% CI)		0.995 (0.703, 1.408)
	Treatment P-value [a]		0.87554
	Interaction P-value [b]		0.53794
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.32 (0.21, 0.43)	7, 0.35 (0.25, 0.46)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.18 (0.06, 0.35)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.CF.KM.S5.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	89 (49.2)	81 (44.3)
	Median Survival Est. (95% CI)	1.51 (0.99, 2.20)	0.99 (0.76, 1.51)
	Hazard Ratio (95% CI)		0.861 (0.637, 1.164)
	Treatment P-value [a]		0.32925
	Interaction P-value [b]		0.53794
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.25 (0.16, 0.36)	8, 0.30 (0.21, 0.39)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.22 (0.12, 0.33)	1, 0.19 (0.07, 0.34)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.CF.KM.S6.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	46 (49.5)	42 (44.2)
	Median Survival Est. (95% CI)	1.31 (0.76, 2.69)	1.28 (0.62, 1.54)
	Hazard Ratio (95% CI)		0.888 (0.585, 1.350)
	Treatment P-value [a]		0.58275
	Interaction P-value [b]		0.83985
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.29 (0.17, 0.42)	2, 0.25 (0.14, 0.38)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.12 (0.02, 0.28)	1, 0.25 (0.14, 0.38)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.CF.KM.S6.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	109 (52.4)	101 (47.6)
	Median Survival Est. (95% CI)	1.77 (1.41, 2.43)	1.45 (1.02, 2.37)
	Hazard Ratio (95% CI)		0.935 (0.713, 1.226)
	Treatment P-value [a]		0.63970
	Interaction P-value [b]		0.83985
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.28 (0.19, 0.37)	13, 0.35 (0.26, 0.43)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.17 (0.07, 0.31)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.CF.KM.S7.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	86 (61.0)	50 (44.6)
	Median Survival Est. (95% CI)	1.08 (0.82, 1.74)	1.51 (1.18, 3.78)
	Hazard Ratio (95% CI)		1.299 (0.916, 1.841)
	Treatment P-value [a]		0.13385
	Interaction P-value [b]		0.03084
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.16 (0.08, 0.27)	5, 0.34 (0.22, 0.46)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.CF.KM.S7.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	43 (49.4)	61 (52.1)
	Median Survival Est. (95% CI)	2.20 (1.41, 5.52)	1.05 (0.79, 1.74)
	Hazard Ratio (95% CI)		0.689 (0.466, 1.018)
	Treatment P-value [a]		0.05651
	Interaction P-value [b]		0.03084
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.36 (0.23, 0.49)	6, 0.25 (0.15, 0.36)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.20 (0.07, 0.38)	1, 0.10 (0.01, 0.31)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Astellas: 7465-CL-0301
Table EORTC15.CF.KM.S7.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	26 (35.6)	32 (41.0)
	Median Survival Est. (95% CI)	5.95 (1.45, NC)	1.28 (0.76, NC)
	Hazard Ratio (95% CI)		0.695 (0.414, 1.167)
	Treatment P-value [a]		0.19023
	Interaction P-value [b]		0.03084
6 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.43 (0.24, 0.61)	4, 0.41 (0.28, 0.54)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.31 (0.13, 0.51)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.CF.KM.S8.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	55 (56.1)	59 (55.1)
	Median Survival Est. (95% CI)	1.08 (0.69, 1.91)	1.15 (0.79, 1.94)
	Hazard Ratio (95% CI)		1.016 (0.703, 1.467)
	Treatment P-value [a]		0.90530
	Interaction P-value [b]		0.61171
6 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.22 (0.12, 0.34)	6, 0.28 (0.18, 0.40)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.CF.KM.S8.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	100 (49.3)	84 (42.0)
	Median Survival Est. (95% CI)	1.77 (1.48, 2.69)	1.48 (0.99, 2.37)
	Hazard Ratio (95% CI)		0.900 (0.673, 1.203)
	Treatment P-value [a]		0.48972
	Interaction P-value [b]		0.61171
6 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.31 (0.22, 0.41)	9, 0.35 (0.26, 0.44)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.21 (0.11, 0.34)	2, 0.27 (0.15, 0.39)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Astellas: 7465-CL-0301
Table EORTC15.CF.KM.S9.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	133 (50.8)	124 (45.9)
	Median Survival Est. (95% CI)	1.74 (1.31, 2.40)	1.45 (1.02, 1.74)
	Hazard Ratio (95% CI)		0.898 (0.703, 1.147)
	Treatment P-value [a]		0.37183
	Interaction P-value [b]		0.50562
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.28 (0.20, 0.36)	13, 0.32 (0.24, 0.39)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.20 (0.11, 0.31)	1, 0.13 (0.04, 0.28)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.CF.KM.S9.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	22 (56.4)	19 (51.4)
	Median Survival Est. (95% CI)	0.99 (0.59, 2.46)	1.25 (0.39, NC)
	Hazard Ratio (95% CI)		1.124 (0.608, 2.079)
	Treatment P-value [a]		0.78288
	Interaction P-value [b]		0.50562
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.31 (0.15, 0.49)	2, 0.35 (0.19, 0.52)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.35 (0.19, 0.52)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.CF.KM.S10.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	34 (55.7)	35 (70.0)
	Median Survival Est. (95% CI)	1.74 (1.22, 2.63)	1.02 (0.76, 1.51)
	Hazard Ratio (95% CI)		0.585 (0.365, 0.939)
	Treatment P-value [a]		0.02623
	Interaction P-value [b]		0.02382
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.25 (0.12, 0.42)	2, 0.14 (0.05, 0.28)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.CF.KM.S10.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	108 (52.2)	90 (41.9)
	Median Survival Est. (95% CI)	1.48 (0.99, 2.20)	1.48 (1.02, 2.37)
	Hazard Ratio (95% CI)		1.103 (0.833, 1.459)
	Treatment P-value [a]		0.49293
	Interaction P-value [b]		0.02382
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.27 (0.19, 0.36)	12, 0.38 (0.30, 0.47)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.17 (0.08, 0.29)	2, 0.23 (0.09, 0.40)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

3.1.2.6 Soziale Funktion

Astellas: 7465-CL-0301
Table EORTC15.SF.KM.S1.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Time Point	Statistics	Enfortumab Vedotin (N=108)	Chemotherapy (N=111)
Overall	No. of Events (%)	63 (58.3)	51 (45.9)
	Median Survival Est. (95% CI)	0.82 (0.56, 1.45)	0.99 (0.76, 1.68)
	Hazard Ratio (95% CI)		0.995 (0.687, 1.440)
	Treatment P-value [a]		0.85733
	Interaction P-value [b]		0.34577
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.25 (0.14, 0.37)	3, 0.28 (0.17, 0.39)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.SF.KM.S1.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Time Point	Statistics	Enfortumab Vedotin (N=193)	Chemotherapy (N=196)
Overall	No. of Events (%)	104 (53.9)	105 (53.6)
	Median Survival Est. (95% CI)	1.08 (0.79, 1.71)	0.85 (0.72, 1.08)
	Hazard Ratio (95% CI)		0.798 (0.608, 1.047)
	Treatment P-value [a]		0.12116
	Interaction P-value [b]		0.34577
6 Months	Patients at Risk, Survival Est. (95% CI)	14, 0.31 (0.23, 0.39)	8, 0.22 (0.14, 0.30)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.12 (0.01, 0.33)	1, 0.14 (0.05, 0.29)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.SF.KM.S2.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Time Point	Statistics	Enfortumab Vedotin (N=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	143 (57.4)	118 (49.4)
	Median Survival Est. (95% CI)	0.99 (0.69, 1.41)	0.82 (0.72, 1.18)
	Hazard Ratio (95% CI)		0.868 (0.680, 1.108)
	Treatment P-value [a]		0.25345
	Interaction P-value [b]		0.83778
6 Months	Patients at Risk, Survival Est. (95% CI)	18, 0.28 (0.21, 0.36)	8, 0.24 (0.17, 0.32)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.SF.KM.S2.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Time Point	Statistics	Enfortumab Vedotin (N=52)	Chemotherapy (N=68)
Overall	No. of Events (%)	24 (46.2)	38 (55.9)
	Median Survival Est. (95% CI)	1.02 (0.49, 1.94)	0.99 (0.72, 1.25)
	Hazard Ratio (95% CI)		0.818 (0.490, 1.365)
	Treatment P-value [a]		0.48766
	Interaction P-value [b]		0.83778
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.34 (0.19, 0.50)	3, 0.21 (0.10, 0.35)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.34 (0.19, 0.50)	1, 0.11 (0.01, 0.32)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.SF.KM.S3.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Male

Time Point	Statistics	Enfortumab Vedotin (N=238)	Chemotherapy (N=232)
Overall	No. of Events (%)	138 (58.0)	116 (50.0)
	Median Survival Est. (95% CI)	0.99 (0.76, 1.28)	0.89 (0.72, 1.18)
	Hazard Ratio (95% CI)		0.916 (0.715, 1.173)
	Treatment P-value [a]		0.49647
	Interaction P-value [b]		0.26530
6 Months	Patients at Risk, Survival Est. (95% CI)	18, 0.27 (0.20, 0.35)	9, 0.25 (0.17, 0.33)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.08 (0.01, 0.24)	1, 0.16 (0.05, 0.33)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.SF.KM.S3.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Gender, Level: Female

Time Point	Statistics	Enfortumab Vedotin (N=63)	Chemotherapy (N=75)
Overall	No. of Events (%)	29 (46.0)	40 (53.3)
	Median Survival Est. (95% CI)	1.22 (0.53, NC)	0.99 (0.76, 1.22)
	Hazard Ratio (95% CI)		0.675 (0.418, 1.089)
	Treatment P-value [a]		0.11310
	Interaction P-value [b]		0.26530
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.36 (0.21, 0.52)	2, 0.20 (0.10, 0.33)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.SF.KM.S4.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	60 (47.6)	60 (46.5)
	Median Survival Est. (95% CI)	1.25 (0.69, 2.23)	0.72 (0.39, 1.05)
	Hazard Ratio (95% CI)		0.690 (0.482, 0.988)
	Treatment P-value [a]		0.04576
	Interaction P-value [b]		0.29901
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.30 (0.19, 0.43)	5, 0.19 (0.10, 0.30)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.SF.KM.S4.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: US

Time Point	Statistics	Enfortumab Vedotin (N=43)	Chemotherapy (N=44)
Overall	No. of Events (%)	18 (41.9)	17 (38.6)
	Median Survival Est. (95% CI)	1.51 (0.46, NC)	1.08 (0.72, NC)
	Hazard Ratio (95% CI)		0.901 (0.463, 1.756)
	Treatment P-value [a]		0.80334
	Interaction P-value [b]		0.29901
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.38 (0.18, 0.57)	0
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.19 (0.02, 0.50)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
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Astellas: 7465-CL-0301
Table EORTC15.SF.KM.S4.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Region, Level: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	89 (67.4)	79 (59.0)
	Median Survival Est. (95% CI)	0.89 (0.59, 1.22)	0.92 (0.76, 1.41)
	Hazard Ratio (95% CI)		1.000 (0.738, 1.355)
	Treatment P-value [a]		0.94504
	Interaction P-value [b]		0.29901
6 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.26 (0.17, 0.35)	6, 0.25 (0.17, 0.34)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.25 (0.17, 0.34)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.SF.KM.S5.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Time Point	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=124)
Overall	No. of Events (%)	77 (64.2)	64 (51.6)
	Median Survival Est. (95% CI)	0.99 (0.59, 1.45)	1.08 (0.82, 1.61)
	Hazard Ratio (95% CI)		1.090 (0.782, 1.520)
	Treatment P-value [a]		0.64690
	Interaction P-value [b]		0.05702
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.23 (0.14, 0.34)	5, 0.32 (0.23, 0.42)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC15.SF.KM.S5.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Time Point	Statistics	Enfortumab Vedotin (N=181)	Chemotherapy (N=183)
Overall	No. of Events (%)	90 (49.7)	92 (50.3)
	Median Survival Est. (95% CI)	1.02 (0.69, 1.74)	0.76 (0.53, 0.99)
	Hazard Ratio (95% CI)		0.710 (0.531, 0.951)
	Treatment P-value [a]		0.02502
	Interaction P-value [b]		0.05702
6 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.34 (0.25, 0.43)	6, 0.16 (0.09, 0.25)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.11 (0.01, 0.33)	1, 0.11 (0.03, 0.23)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.SF.KM.S6.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Time Point	Statistics	Enfortumab Vedotin (N=93)	Chemotherapy (N=95)
Overall	No. of Events (%)	47 (50.5)	45 (47.4)
	Median Survival Est. (95% CI)	0.89 (0.59, 1.74)	0.76 (0.53, 1.28)
	Hazard Ratio (95% CI)		0.772 (0.512, 1.163)
	Treatment P-value [a]		0.24065
	Interaction P-value [b]		0.54068
6 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.30 (0.18, 0.43)	1, 0.18 (0.09, 0.31)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.26 (0.13, 0.40)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.SF.KM.S6.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	120 (57.7)	111 (52.4)
	Median Survival Est. (95% CI)	1.02 (0.79, 1.45)	0.99 (0.76, 1.18)
	Hazard Ratio (95% CI)		0.898 (0.693, 1.163)
	Treatment P-value [a]		0.42875
	Interaction P-value [b]		0.54068
6 Months	Patients at Risk, Survival Est. (95% CI)	15, 0.29 (0.21, 0.37)	10, 0.25 (0.18, 0.33)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.17 (0.06, 0.33)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.SF.KM.S7.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	85 (60.3)	56 (50.0)
	Median Survival Est. (95% CI)	0.82 (0.59, 1.22)	1.05 (0.76, 1.61)
	Hazard Ratio (95% CI)		1.071 (0.764, 1.502)
	Treatment P-value [a]		0.68337
	Interaction P-value [b]		0.14897
6 Months	Patients at Risk, Survival Est. (95% CI)	10, 0.26 (0.17, 0.36)	5, 0.24 (0.14, 0.35)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.SF.KM.S7.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Time Point	Statistics	Enfortumab Vedotin (N=87)	Chemotherapy (N=117)
Overall	No. of Events (%)	50 (57.5)	58 (49.6)
	Median Survival Est. (95% CI)	0.85 (0.53, 1.87)	0.76 (0.36, 1.08)
	Hazard Ratio (95% CI)		0.837 (0.573, 1.224)
	Treatment P-value [a]		0.45540
	Interaction P-value [b]		0.14897
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.30 (0.19, 0.42)	3, 0.27 (0.17, 0.39)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.10 (0.01, 0.32)	1, 0.27 (0.17, 0.39)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.SF.KM.S7.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Time Point	Statistics	Enfortumab Vedotin (N=73)	Chemotherapy (N=78)
Overall	No. of Events (%)	32 (43.8)	42 (53.8)
	Median Survival Est. (95% CI)	1.74 (0.95, 6.83)	0.82 (0.53, 1.51)
	Hazard Ratio (95% CI)		0.609 (0.384, 0.964)
	Treatment P-value [a]		0.02838
	Interaction P-value [b]		0.14897
6 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.32 (0.16, 0.50)	3, 0.19 (0.09, 0.31)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.SF.KM.S8.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Time Point	Statistics	Enfortumab Vedotin (N=98)	Chemotherapy (N=107)
Overall	No. of Events (%)	54 (55.1)	67 (62.6)
	Median Survival Est. (95% CI)	1.02 (0.72, 1.54)	0.76 (0.53, 0.99)
	Hazard Ratio (95% CI)		0.719 (0.502, 1.029)
	Treatment P-value [a]		0.06791
	Interaction P-value [b]		0.19738
6 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.29 (0.18, 0.40)	4, 0.19 (0.11, 0.29)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.SF.KM.S8.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	113 (55.7)	89 (44.5)
	Median Survival Est. (95% CI)	0.99 (0.59, 1.71)	1.05 (0.76, 1.28)
	Hazard Ratio (95% CI)		0.969 (0.733, 1.280)
	Treatment P-value [a]		0.82409
	Interaction P-value [b]		0.19738
6 Months	Patients at Risk, Survival Est. (95% CI)	14, 0.29 (0.20, 0.38)	7, 0.26 (0.18, 0.36)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.09 (0.01, 0.28)	1, 0.26 (0.18, 0.36)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.SF.KM.S9.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Time Point	Statistics	Enfortumab Vedotin (N=262)	Chemotherapy (N=270)
Overall	No. of Events (%)	144 (55.0)	136 (50.4)
	Median Survival Est. (95% CI)	0.99 (0.69, 1.28)	0.92 (0.76, 1.18)
	Hazard Ratio (95% CI)		0.846 (0.669, 1.071)
	Treatment P-value [a]		0.17045
	Interaction P-value [b]		0.67784
6 Months	Patients at Risk, Survival Est. (95% CI)	21, 0.30 (0.23, 0.38)	8, 0.22 (0.15, 0.29)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.10 (0.01, 0.30)	0

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.SF.KM.S9.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	23 (59.0)	20 (54.1)
	Median Survival Est. (95% CI)	1.41 (0.69, 5.42)	0.76 (0.36, 10.87)
	Hazard Ratio (95% CI)		0.971 (0.532, 1.771)
	Treatment P-value [a]		0.97898
	Interaction P-value [b]		0.67784
6 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.19 (0.05, 0.41)	3, 0.35 (0.19, 0.53)
12 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.18 (0.02, 0.48)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

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Table EORTC15.SF.KM.S10.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	42 (68.9)	32 (64.0)
	Median Survival Est. (95% CI)	0.69 (0.53, 1.41)	0.76 (0.33, 1.51)
	Hazard Ratio (95% CI)		0.842 (0.531, 1.333)
	Treatment P-value [a]		0.44750
	Interaction P-value [b]		0.89989
6 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.20 (0.09, 0.33)	2, 0.15 (0.05, 0.29)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 07MAY2021 10:06
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC15.SF.KM.S10.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Time Point	Statistics	Enfortumab Vedotin (N=207)	Chemotherapy (N=215)
Overall	No. of Events (%)	106 (51.2)	105 (48.8)
	Median Survival Est. (95% CI)	0.99 (0.69, 1.54)	0.89 (0.76, 1.18)
	Hazard Ratio (95% CI)		0.871 (0.665, 1.141)
	Treatment P-value [a]		0.31953
	Interaction P-value [b]		0.89989
6 Months	Patients at Risk, Survival Est. (95% CI)	16, 0.32 (0.24, 0.41)	8, 0.25 (0.17, 0.33)
12 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.20 (0.11, 0.32)	1, 0.17 (0.05, 0.33)

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level. The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a 2-sided unstratified log-rank test.
[b] Based on an unstratified Cox proportional hazard model including adjustment for subgroup and treatment*subgroup interaction.

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Analysis Plan: 15FEB2021 Confidential

3.1.3 MMRM-Modell

3.1.3.1 Globaler Gesundheitsstatus

Table EORTC.QL.MM.S1.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Global Health Status (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Age Group 1

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
<65 years	N, n	108, 85	111, 68	
	Baseline Mean (SD)	62.25 (19.27)	66.91 (19.21)	
	Change from Baseline LS Mean (SE)	-1.28 (1.28)	-3.96 (1.43)	2.68 (-1.09, 6.46)
	Treatment P-value			0.16300
	Hedge's g (95% CI)			0.18 (-0.14, 0.49)
>=65 years	N, n	193, 147	196, 128	
	Baseline Mean (SD)	65.76 (18.99)	67.32 (18.13)	
	Change from Baseline LS Mean (SE)	-4.34 (0.98)	-9.42 (1.07)	5.09 (2.23, 7.94)
	Treatment P-value			0.00050
	Hedge's g (95% CI)			0.31 (0.08, 0.55)
	Interaction P-value [b]			0.23777

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.QL.MM.S2.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Global Health Status (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Age Group 2

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
<75 years	N, n	249, 195	239, 150	
	Baseline Mean (SD)	63.85 (19.37)	67.00 (18.92)	
	Change from Baseline LS Mean (SE)	-2.68 (0.85)	-6.75 (0.98)	4.07 (1.51, 6.62)
	Treatment P-value			0.00191
	Hedge's g (95% CI)			0.25 (0.04, 0.47)
>=75 years	N, n	52, 37	68, 46	
	Baseline Mean (SD)	67.79 (17.70)	67.75 (17.09)	
	Change from Baseline LS Mean (SE)	-6.31 (2.02)	-9.89 (1.80)	3.58 (-1.75, 8.90)
	Treatment P-value			0.18766
	Hedge's g (95% CI)			0.23 (-0.20, 0.66)
	Interaction P-value [b]			0.79636

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.QL.MM.S3.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Global Health Status (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Gender

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Male	N, n	238, 182	232, 150	
	Baseline Mean (SD)	64.93 (18.87)	66.78 (18.27)	
	Change from Baseline LS Mean (SE)	-3.67 (0.89)	-7.20 (0.99)	3.53 (0.92, 6.15)
	Treatment P-value			0.00820
	Hedge's g (95% CI)			0.22 (0.01, 0.44)
Female	N, n	63, 50	75, 46	
	Baseline Mean (SD)	62.83 (20.15)	68.48 (19.24)	
	Change from Baseline LS Mean (SE)	-1.53 (1.70)	-8.38 (1.80)	6.85 (1.99, 11.72)
	Treatment P-value			0.00587
	Hedge's g (95% CI)			0.41 (0.01, 0.81)
	Interaction P-value [b]			0.54596

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.QL.MM.S4.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Global Health Status (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Region

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Western Europe	N, n	126, 90	129, 70	
	Baseline Mean (SD)	64.91 (18.76)	64.64 (20.73)	
	Change from Baseline LS Mean (SE)	-2.24 (1.27)	-8.97 (1.47)	6.72 (2.91, 10.54)
	Treatment P-value			0.00058
	Hedge's g (95% CI)			0.43 (0.11, 0.74)
US	N, n	43, 28	44, 24	
	Baseline Mean (SD)	75.89 (18.33)	73.61 (15.28)	
	Change from Baseline LS Mean (SE)	-6.91 (2.34)	-6.36 (2.48)	-0.55 (-7.24, 6.14)
	Treatment P-value			0.87170
	Hedge's g (95% CI)			-0.04 (-0.57, 0.50)

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.QL.MM.S4.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Global Health Status (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Region

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Rest of the World	N, n	132, 114	134, 102	
	Baseline Mean (SD)	61.33 (18.65)	67.40 (17.24)	
	Change from Baseline LS Mean (SE)	-3.35 (1.11)	-6.78 (1.19)	3.44 (0.24, 6.63)
	Treatment P-value			0.03525
	Hedge's g (95% CI)			0.21 (-0.06, 0.48)
	Interaction P-value [b]			0.30329

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.QL.MM.S5.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Global Health Status (Week 1 to Week 24) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
0	N, n	120, 102	124, 92	
	Baseline Mean (SD)	69.61 (17.58)	71.47 (17.26)	
	Change from Baseline LS Mean (SE)	-5.35 (1.16)	-6.16 (1.23)	0.82 (-2.51, 4.14)
	Treatment P-value			0.62970
	Hedge's g (95% CI)			0.05 (-0.23, 0.33)
1	N, n	181, 130	183, 104	
	Baseline Mean (SD)	60.45 (19.39)	63.38 (18.74)	
	Change from Baseline LS Mean (SE)	-1.33 (1.06)	-8.61 (1.19)	7.28 (4.15, 10.41)
	Treatment P-value			<.00001
	Hedge's g (95% CI)			0.44 (0.18, 0.70)
	Interaction P-value [b]			0.03222

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.QL.MM.S6.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Global Health Status (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Yes	N, n	93, 63	95, 52	
	Baseline Mean (SD)	58.47 (19.37)	65.71 (18.28)	
	Change from Baseline LS Mean (SE)	0.94 (1.52)	-9.62 (1.70)	10.57 (6.08, 15.05)
	Treatment P-value			<.00001
	Hedge's g (95% CI)			0.58 (0.21, 0.95)
No	N, n	208, 169	212, 144	
	Baseline Mean (SD)	66.72 (18.60)	67.71 (18.57)	
	Change from Baseline LS Mean (SE)	-4.66 (0.92)	-6.71 (1.00)	2.04 (-0.63, 4.72)
	Treatment P-value			0.13398
	Hedge's g (95% CI)			0.13 (-0.09, 0.36)
	Interaction P-value [b]			0.10712

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.QL.MM.S7.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Global Health Status (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Paclitaxel	N, n	141, 115	112, 72	
	Baseline Mean (SD)	62.17 (18.84)	70.02 (16.23)	
	Change from Baseline LS Mean (SE)	-2.39 (1.11)	-7.57 (1.41)	5.17 (1.65, 8.70)
	Treatment P-value			0.00409
	Hedge's g (95% CI)			0.33 (0.03, 0.62)
Docetaxel	N, n	87, 65	117, 77	
	Baseline Mean (SD)	68.21 (18.27)	68.94 (17.76)	
	Change from Baseline LS Mean (SE)	-5.85 (1.49)	-7.85 (1.40)	2.00 (-2.01, 6.00)
	Treatment P-value			0.32838
	Hedge's g (95% CI)			0.12 (-0.20, 0.45)

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.QL.MM.S7.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Global Health Status (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Vinflunine	N, n	73, 52	78, 47	
	Baseline Mean (SD)	64.90 (20.37)	59.93 (21.11)	
	Change from Baseline LS Mean (SE)	-1.57 (1.71)	-6.52 (1.79)	4.95 (0.09, 9.82)
	Treatment P-value			0.04573
	Hedge's g (95% CI)			0.30 (-0.09, 0.70)
	Interaction P-value [b]			0.46018

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.QL.MM.S8.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Global Health Status (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Primary Site of Tumor

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Upper Tract	N, n	98, 75	107, 76	
	Baseline Mean (SD)	62.22 (19.34)	68.20 (15.68)	
	Change from Baseline LS Mean (SE)	-2.69 (1.38)	-8.55 (1.38)	5.87 (2.04, 9.70)
	Treatment P-value			0.00275
	Hedge's g (95% CI)			0.35 (0.03, 0.67)
Other	N, n	203, 157	200, 120	
	Baseline Mean (SD)	65.55 (18.99)	66.53 (20.07)	
	Change from Baseline LS Mean (SE)	-3.48 (0.96)	-6.75 (1.11)	3.27 (0.38, 6.16)
	Treatment P-value			0.02687
	Hedge's g (95% CI)			0.21 (-0.03, 0.45)
	Interaction P-value [b]			0.71107

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.QL.MM.S9.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Global Health Status (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
1-2 lines	N, n	262, 203	270, 169	
	Baseline Mean (SD)	63.96 (19.18)	67.50 (18.82)	
	Change from Baseline LS Mean (SE)	-3.12 (0.85)	-7.83 (0.93)	4.71 (2.23, 7.19)
	Treatment P-value			0.00021
	Hedge's g (95% CI)			0.29 (0.09, 0.50)
>=3 lines	N, n	39, 29	37, 27	
	Baseline Mean (SD)	68.10 (18.64)	65.12 (16.18)	
	Change from Baseline LS Mean (SE)	-3.74 (2.14)	-5.14 (2.34)	1.40 (-4.83, 7.63)
	Treatment P-value			0.65919
	Hedge's g (95% CI)			0.09 (-0.43, 0.61)
	Interaction P-value [b]			0.59893

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.QL.MM.S10.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Global Health Status (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Best Response to Prior CPI

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Responder	N, n	61, 49	50, 34	
	Baseline Mean (SD)	70.24 (16.49)	67.65 (20.28)	
	Change from Baseline LS Mean (SE)	-7.04 (1.68)	-9.37 (2.05)	2.33 (-2.88, 7.54)
	Treatment P-value			0.38027
	Hedge's g (95% CI)			0.16 (-0.28, 0.59)
Non-responder	N, n	207, 156	215, 136	
	Baseline Mean (SD)	62.87 (19.03)	66.54 (18.37)	
	Change from Baseline LS Mean (SE)	-1.66 (0.96)	-6.64 (1.04)	4.98 (2.20, 7.77)
	Treatment P-value			0.00049
	Hedge's g (95% CI)			0.30 (0.07, 0.53)
	Interaction P-value [b]			0.86176

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
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3.1.3.2 Körperliche Funktion

Astellas: 7465-CL-0301
Table EORTC.PF.MM.S1.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Physical Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Age Group 1

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
<65 years	N, n	108, 85	111, 68	
	Baseline Mean (SD)	76.47 (20.09)	79.41 (20.24)	
	Change from Baseline LS Mean (SE)	-1.57 (1.37)	-2.30 (1.53)	0.73 (-3.31, 4.78)
	Treatment P-value			0.72229
	Hedge's g (95% CI)			0.05 (-0.27, 0.37)
>=65 years	N, n	193, 147	196, 128	
	Baseline Mean (SD)	76.05 (21.56)	76.46 (20.25)	
	Change from Baseline LS Mean (SE)	-3.39 (1.05)	-8.11 (1.14)	4.73 (1.68, 7.77)
	Treatment P-value			0.00242
	Hedge's g (95% CI)			0.30 (0.06, 0.53)
	Interaction P-value [b]			0.05659

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.PF.MM.S2.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Physical Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Age Group 2

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
<75 years	N, n	249, 195	239, 150	
	Baseline Mean (SD)	76.44 (20.80)	78.13 (21.14)	
	Change from Baseline LS Mean (SE)	-2.38 (0.92)	-4.97 (1.05)	2.59 (-0.15, 5.33)
	Treatment P-value			0.06436
	Hedge's g (95% CI)			0.17 (-0.04, 0.38)
>=75 years	N, n	52, 37	68, 46	
	Baseline Mean (SD)	74.95 (22.24)	75.36 (17.03)	
	Change from Baseline LS Mean (SE)	-4.57 (2.13)	-9.77 (1.91)	5.20 (-0.42, 10.82)
	Treatment P-value			0.06974
	Hedge's g (95% CI)			0.30 (-0.13, 0.73)
	Interaction P-value [b]			0.30847

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.PF.MM.S3.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Physical Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Gender

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Male	N, n	238, 182	232, 150	
	Baseline Mean (SD)	77.25 (20.10)	77.60 (21.13)	
	Change from Baseline LS Mean (SE)	-3.19 (0.96)	-5.79 (1.07)	2.60 (-0.22, 5.42)
	Treatment P-value			0.07061
	Hedge's g (95% CI)			0.16 (-0.05, 0.38)
Female	N, n	63, 50	75, 46	
	Baseline Mean (SD)	72.40 (23.79)	77.10 (17.25)	
	Change from Baseline LS Mean (SE)	-1.02 (1.83)	-6.99 (1.93)	5.97 (0.75, 11.20)
	Treatment P-value			0.02512
	Hedge's g (95% CI)			0.45 (0.05, 0.85)
	Interaction P-value [b]			0.29539

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.PF.MM.S4.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Physical Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Region

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Western Europe	N, n	126, 90	129, 70	
	Baseline Mean (SD)	74.74 (22.71)	73.52 (23.62)	
	Change from Baseline LS Mean (SE)	-2.46 (1.36)	-7.86 (1.57)	5.40 (1.32, 9.48)
	Treatment P-value			0.00955
	Hedge's g (95% CI)			0.33 (0.02, 0.64)
US	N, n	43, 28	44, 24	
	Baseline Mean (SD)	83.57 (16.07)	80.00 (16.33)	
	Change from Baseline LS Mean (SE)	-1.89 (2.47)	-4.15 (2.66)	2.26 (-4.89, 9.40)
	Treatment P-value			0.53511
	Hedge's g (95% CI)			0.18 (-0.36, 0.72)

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.PF.MM.S4.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Physical Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Region

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Rest of the World	N, n	132, 114	134, 102	
	Baseline Mean (SD)	75.56 (20.43)	79.61 (18.24)	
	Change from Baseline LS Mean (SE)	-3.22 (1.20)	-5.32 (1.28)	2.11 (-1.33, 5.55)
	Treatment P-value			0.22934
	Hedge's g (95% CI)			0.14 (-0.13, 0.40)
	Interaction P-value [b]			0.38253

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.PF.MM.S5.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Physical Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
0	N, n	120, 102	124, 92	
	Baseline Mean (SD)	85.29 (14.14)	83.99 (15.88)	
	Change from Baseline LS Mean (SE)	-4.43 (1.23)	-4.25 (1.31)	-0.18 (-3.71, 3.34)
	Treatment P-value			0.91938
	Hedge's g (95% CI)			-0.01 (-0.29, 0.27)
1	N, n	181, 130	183, 104	
	Baseline Mean (SD)	69.08 (22.72)	71.73 (21.95)	
	Change from Baseline LS Mean (SE)	-1.18 (1.11)	-7.57 (1.26)	6.39 (3.09, 9.69)
	Treatment P-value			0.00016
	Hedge's g (95% CI)			0.38 (0.12, 0.64)
	Interaction P-value [b]			0.02097

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.PF.MM.S6.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Physical Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Yes	N, n	93, 63	95, 52	
	Baseline Mean (SD)	70.16 (20.46)	78.21 (18.06)	
	Change from Baseline LS Mean (SE)	0.91 (1.62)	-9.56 (1.82)	10.47 (5.67, 15.26)
	Treatment P-value			0.00002
	Hedge's g (95% CI)			0.58 (0.21, 0.95)
No	N, n	208, 169	212, 144	
	Baseline Mean (SD)	78.46 (20.80)	77.22 (21.03)	
	Change from Baseline LS Mean (SE)	-3.99 (0.99)	-4.87 (1.08)	0.87 (-2.01, 3.75)
	Treatment P-value			0.55291
	Hedge's g (95% CI)			0.06 (-0.16, 0.28)
	Interaction P-value [b]			0.07346

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.PF.MM.S7.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Physical Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Paclitaxel	N, n	141, 115	112, 72	
	Baseline Mean (SD)	75.71 (20.39)	80.65 (18.42)	
	Change from Baseline LS Mean (SE)	-2.60 (1.20)	-5.81 (1.51)	3.20 (-0.58, 6.99)
	Treatment P-value			0.09696
	Hedge's g (95% CI)			0.21 (-0.08, 0.50)
Docetaxel	N, n	87, 65	117, 77	
	Baseline Mean (SD)	78.87 (20.43)	78.44 (18.41)	
	Change from Baseline LS Mean (SE)	-2.97 (1.59)	-5.48 (1.49)	2.50 (-1.78, 6.79)
	Treatment P-value			0.25169
	Hedge's g (95% CI)			0.17 (-0.16, 0.50)

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.PF.MM.S7.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Physical Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Vinflunine	N, n	73, 52	78, 47	
	Baseline Mean (SD)	73.97 (22.99)	71.06 (24.37)	
	Change from Baseline LS Mean (SE)	-2.52 (1.81)	-7.37 (1.92)	4.84 (-0.34, 10.03)
	Treatment P-value			0.06674
	Hedge's g (95% CI)			0.28 (-0.11, 0.67)
	Interaction P-value [b]			0.44347

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.PF.MM.S8.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Physical Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Primary Site of Tumor

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Upper Tract	N, n	98, 75	107, 76	
	Baseline Mean (SD)	73.87 (22.83)	77.54 (20.71)	
	Change from Baseline LS Mean (SE)	-2.01 (1.49)	-6.30 (1.49)	4.30 (0.16, 8.43)
	Treatment P-value			0.04163
	Hedge's g (95% CI)			0.27 (-0.05, 0.59)
Other	N, n	203, 157	200, 120	
	Baseline Mean (SD)	77.32 (20.04)	77.44 (20.03)	
	Change from Baseline LS Mean (SE)	-3.09 (1.04)	-5.91 (1.20)	2.82 (-0.29, 5.93)
	Treatment P-value			0.07582
	Hedge's g (95% CI)			0.18 (-0.05, 0.42)
	Interaction P-value [b]			0.83321

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.PF.MM.S9.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Physical Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
1-2 lines	N, n	262, 203	270, 169	
	Baseline Mean (SD)	75.63 (21.46)	78.07 (19.44)	
	Change from Baseline LS Mean (SE)	-2.38 (0.91)	-6.99 (1.00)	4.61 (1.95, 7.27)
	Treatment P-value			0.00073
	Hedge's g (95% CI)			0.30 (0.09, 0.50)
>=3 lines	N, n	39, 29	37, 27	
	Baseline Mean (SD)	80.23 (17.13)	73.83 (24.80)	
	Change from Baseline LS Mean (SE)	-4.92 (2.31)	-0.28 (2.50)	-4.64 (-11.33, 2.05)
	Treatment P-value			0.17340
	Hedge's g (95% CI)			-0.28 (-0.80, 0.24)
	Interaction P-value [b]			0.03880

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.PF.MM.S10.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Physical Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Best Response to Prior CPI

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Responder	N, n	61, 49	50, 34	
	Baseline Mean (SD)	81.63 (17.51)	79.80 (20.86)	
	Change from Baseline LS Mean (SE)	-6.90 (1.84)	-7.84 (2.23)	0.95 (-4.74, 6.63)
	Treatment P-value			0.74347
	Hedge's g (95% CI)			0.06 (-0.38, 0.49)
Non-responder	N, n	207, 156	215, 136	
	Baseline Mean (SD)	74.44 (21.55)	76.08 (20.36)	
	Change from Baseline LS Mean (SE)	-1.43 (1.05)	-5.32 (1.14)	3.89 (0.85, 6.94)
	Treatment P-value			0.01231
	Hedge's g (95% CI)			0.26 (0.03, 0.49)
	Interaction P-value [b]			0.66630

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

3.1.3.3 Rollenfunktion

Astellas: 7465-CL-0301
Table EORTC.RF.MM.S1.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Role Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Age Group 1

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
<65 years	N, n	108, 85	111, 68	
	Baseline Mean (SD)	75.49 (25.14)	76.23 (25.48)	
	Change from Baseline LS Mean (SE)	-7.23 (1.94)	-8.38 (2.16)	1.15 (-4.56, 6.86)
	Treatment P-value			0.69326
	Hedge's g (95% CI)			0.05 (-0.27, 0.37)
>=65 years	N, n	193, 147	196, 128	
	Baseline Mean (SD)	75.96 (27.94)	75.39 (25.36)	
	Change from Baseline LS Mean (SE)	-6.89 (1.48)	-12.91 (1.61)	6.02 (1.72, 10.33)
	Treatment P-value			0.00615
	Hedge's g (95% CI)			0.26 (0.03, 0.50)
	Interaction P-value [b]			0.08107

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.RF.MM.S2.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Role Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Age Group 2

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
<75 years	N, n	249, 195	239, 150	
	Baseline Mean (SD)	74.87 (27.93)	75.56 (25.52)	
	Change from Baseline LS Mean (SE)	-6.33 (1.29)	-10.32 (1.48)	3.99 (0.15, 7.83)
	Treatment P-value			0.04195
	Hedge's g (95% CI)			0.17 (-0.04, 0.39)
>=75 years	N, n	52, 37	68, 46	
	Baseline Mean (SD)	80.63 (20.23)	76.09 (25.01)	
	Change from Baseline LS Mean (SE)	-10.85 (2.99)	-14.66 (2.70)	3.81 (-4.11, 11.74)
	Treatment P-value			0.34489
	Hedge's g (95% CI)			0.16 (-0.27, 0.59)
	Interaction P-value [b]			0.91324

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.RF.MM.S3.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Role Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Gender

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Male	N, n	238, 182	232, 150	
	Baseline Mean (SD)	76.28 (27.21)	76.00 (25.72)	
	Change from Baseline LS Mean (SE)	-7.79 (1.34)	-10.79 (1.48)	3.01 (-0.92, 6.93)
	Treatment P-value			0.13297
	Hedge's g (95% CI)			0.13 (-0.09, 0.34)
Female	N, n	63, 50	75, 46	
	Baseline Mean (SD)	74.00 (25.90)	74.64 (24.28)	
	Change from Baseline LS Mean (SE)	-4.17 (2.55)	-13.04 (2.69)	8.86 (1.58, 16.15)
	Treatment P-value			0.01720
	Hedge's g (95% CI)			0.43 (0.02, 0.83)
	Interaction P-value [b]			0.23030

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.RF.MM.S4.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Role Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Region

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Western Europe	N, n	126, 90	129, 70	
	Baseline Mean (SD)	73.89 (28.60)	71.19 (30.29)	
	Change from Baseline LS Mean (SE)	-6.91 (1.87)	-17.03 (2.16)	10.13 (4.51, 15.75)
	Treatment P-value			0.00044
	Hedge's g (95% CI)			0.41 (0.10, 0.73)
US	N, n	43, 28	44, 24	
	Baseline Mean (SD)	83.93 (23.34)	85.42 (21.60)	
	Change from Baseline LS Mean (SE)	-9.46 (3.42)	-15.60 (3.68)	6.15 (-3.73, 16.02)
	Treatment P-value			0.22201
	Hedge's g (95% CI)			0.28 (-0.26, 0.82)

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.RF.MM.S4.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Role Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Region

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Rest of the World	N, n	132, 114	134, 102	
	Baseline Mean (SD)	75.29 (26.16)	76.47 (21.67)	
	Change from Baseline LS Mean (SE)	-6.60 (1.65)	-6.58 (1.75)	-0.02 (-4.75, 4.71)
	Treatment P-value			0.99391
	Hedge's g (95% CI)			-0.00 (-0.27, 0.27)
	Interaction P-value [b]			0.02478

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.RF.MM.S5.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Role Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
0	N, n	120, 102	124, 92	
	Baseline Mean (SD)	84.97 (20.51)	82.07 (21.29)	
	Change from Baseline LS Mean (SE)	-8.79 (1.73)	-9.68 (1.84)	0.90 (-4.07, 5.86)
	Treatment P-value			0.72239
	Hedge's g (95% CI)			0.04 (-0.24, 0.32)
1	N, n	181, 130	183, 104	
	Baseline Mean (SD)	68.59 (29.10)	70.03 (27.32)	
	Change from Baseline LS Mean (SE)	-5.36 (1.57)	-12.63 (1.77)	7.28 (2.62, 11.93)
	Treatment P-value			0.00226
	Hedge's g (95% CI)			0.30 (0.04, 0.56)
	Interaction P-value [b]			0.16277

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.RF.MM.S6.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Role Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Yes	N, n	93, 63	95, 52	
	Baseline Mean (SD)	70.11 (27.13)	75.32 (23.68)	
	Change from Baseline LS Mean (SE)	-2.63 (2.27)	-14.86 (2.56)	12.23 (5.52, 18.95)
	Treatment P-value			0.00038
	Hedge's g (95% CI)			0.49 (0.12, 0.86)
No	N, n	208, 169	212, 144	
	Baseline Mean (SD)	77.91 (26.57)	75.81 (25.99)	
	Change from Baseline LS Mean (SE)	-8.55 (1.39)	-10.08 (1.51)	1.53 (-2.49, 5.56)
	Treatment P-value			0.45434
	Hedge's g (95% CI)			0.07 (-0.15, 0.29)
	Interaction P-value [b]			0.15890

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.RF.MM.S7.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Role Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Paclitaxel	N, n	141, 115	112, 72	
	Baseline Mean (SD)	74.93 (26.53)	79.40 (22.11)	
	Change from Baseline LS Mean (SE)	-6.55 (1.65)	-8.64 (2.09)	2.09 (-3.14, 7.32)
	Treatment P-value			0.43293
	Hedge's g (95% CI)			0.09 (-0.20, 0.39)
Docetaxel	N, n	87, 65	117, 77	
	Baseline Mean (SD)	78.72 (25.60)	77.27 (22.28)	
	Change from Baseline LS Mean (SE)	-8.16 (2.20)	-12.24 (2.07)	4.09 (-1.86, 10.03)
	Treatment P-value			0.17717
	Hedge's g (95% CI)			0.19 (-0.14, 0.52)

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.RF.MM.S7.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Role Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Vinflunine	N, n	73, 52	78, 47	
	Baseline Mean (SD)	74.04 (29.41)	67.38 (32.41)	
	Change from Baseline LS Mean (SE)	-6.25 (2.52)	-13.93 (2.65)	7.68 (0.49, 14.87)
	Treatment P-value			0.03630
	Hedge's g (95% CI)			0.30 (-0.09, 0.69)
	Interaction P-value [b]			0.13415

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.RF.MM.S8.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Role Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Primary Site of Tumor

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Upper Tract	N, n	98, 75	107, 76	
	Baseline Mean (SD)	72.89 (27.37)	76.54 (25.27)	
	Change from Baseline LS Mean (SE)	-5.40 (2.07)	-12.80 (2.07)	7.39 (1.64, 13.14)
	Treatment P-value			0.01190
	Hedge's g (95% CI)			0.31 (-0.01, 0.63)
Other	N, n	203, 157	200, 120	
	Baseline Mean (SD)	77.18 (26.64)	75.14 (25.47)	
	Change from Baseline LS Mean (SE)	-7.82 (1.45)	-10.34 (1.67)	2.52 (-1.81, 6.86)
	Treatment P-value			0.25363
	Hedge's g (95% CI)			0.11 (-0.13, 0.35)
	Interaction P-value [b]			0.52114

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.RF.MM.S9.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Role Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
1-2 lines	N, n	262, 203	270, 169	
	Baseline Mean (SD)	75.29 (27.67)	75.94 (25.06)	
	Change from Baseline LS Mean (SE)	-6.95 (1.28)	-12.13 (1.40)	5.18 (1.46, 8.90)
	Treatment P-value			0.00644
	Hedge's g (95% CI)			0.22 (0.02, 0.43)
>=3 lines	N, n	39, 29	37, 27	
	Baseline Mean (SD)	79.31 (20.73)	74.07 (27.48)	
	Change from Baseline LS Mean (SE)	-7.43 (3.21)	-6.15 (3.51)	-1.28 (-10.63, 8.07)
	Treatment P-value			0.78756
	Hedge's g (95% CI)			-0.06 (-0.57, 0.46)
	Interaction P-value [b]			0.34125

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.RF.MM.S10.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Role Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Best Response to Prior CPI

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Responder	N, n	61, 49	50, 34	
	Baseline Mean (SD)	79.59 (22.63)	76.96 (25.63)	
	Change from Baseline LS Mean (SE)	-9.37 (2.59)	-12.39 (3.15)	3.01 (-5.00, 11.03)
	Treatment P-value			0.46016
	Hedge's g (95% CI)			0.13 (-0.31, 0.56)
Non-responder	N, n	207, 156	215, 136	
	Baseline Mean (SD)	73.82 (28.34)	73.90 (25.72)	
	Change from Baseline LS Mean (SE)	-5.40 (1.48)	-10.66 (1.61)	5.26 (0.97, 9.56)
	Treatment P-value			0.01651
	Hedge's g (95% CI)			0.23 (-0.00, 0.46)
	Interaction P-value [b]			0.80967

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

3.1.3.4 Emotionale Funktion

Astellas: 7465-CL-0301
Table EORTC.EF.MM.S1.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Emotional Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Age Group 1

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
<65 years	N, n	108, 85	111, 68	
	Baseline Mean (SD)	75.00 (23.54)	75.37 (21.71)	
	Change from Baseline LS Mean (SE)	4.01 (1.30)	1.27 (1.45)	2.74 (-1.09, 6.57)
	Treatment P-value			0.16072
	Hedge's g (95% CI)			0.18 (-0.14, 0.50)
>=65 years	N, n	193, 147	196, 128	
	Baseline Mean (SD)	79.31 (19.00)	78.84 (19.59)	
	Change from Baseline LS Mean (SE)	0.23 (1.00)	-2.60 (1.09)	2.82 (-0.09, 5.74)
	Treatment P-value			0.05720
	Hedge's g (95% CI)			0.17 (-0.06, 0.41)
	Interaction P-value [b]			0.86443

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.EF.MM.S2.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Emotional Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Age Group 2

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
<75 years	N, n	249, 195	239, 150	
	Baseline Mean (SD)	77.48 (20.92)	76.44 (21.58)	
	Change from Baseline LS Mean (SE)	1.99 (0.87)	0.46 (1.00)	1.53 (-1.07, 4.13)
	Treatment P-value			0.24880
	Hedge's g (95% CI)			0.10 (-0.12, 0.31)
>=75 years	N, n	52, 37	68, 46	
	Baseline Mean (SD)	79.05 (20.57)	81.52 (15.31)	
	Change from Baseline LS Mean (SE)	-0.46 (2.02)	-6.83 (1.80)	6.37 (1.05, 11.69)
	Treatment P-value			0.01912
	Hedge's g (95% CI)			0.41 (-0.03, 0.84)
	Interaction P-value [b]			0.22521

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.EF.MM.S3.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Emotional Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Gender

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Male	N, n	238, 182	232, 150	
	Baseline Mean (SD)	79.40 (20.33)	78.11 (20.58)	
	Change from Baseline LS Mean (SE)	0.78 (0.91)	-1.08 (1.01)	1.87 (-0.80, 4.53)
	Treatment P-value			0.16925
	Hedge's g (95% CI)			0.12 (-0.10, 0.33)
Female	N, n	63, 50	75, 46	
	Baseline Mean (SD)	71.67 (21.69)	76.09 (19.77)	
	Change from Baseline LS Mean (SE)	4.70 (1.72)	-1.58 (1.80)	6.29 (1.39, 11.19)
	Treatment P-value			0.01205
	Hedge's g (95% CI)			0.39 (-0.01, 0.79)
	Interaction P-value [b]			0.49393

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.EF.MM.S4.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Emotional Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Region

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Western Europe	N, n	126, 90	129, 70	
	Baseline Mean (SD)	78.89 (21.02)	73.81 (22.98)	
	Change from Baseline LS Mean (SE)	2.07 (1.28)	-2.85 (1.48)	4.92 (1.08, 8.76)
	Treatment P-value			0.01221
	Hedge's g (95% CI)			0.29 (-0.02, 0.60)
US	N, n	43, 28	44, 24	
	Baseline Mean (SD)	76.49 (20.92)	79.17 (17.38)	
	Change from Baseline LS Mean (SE)	-0.11 (2.33)	-1.59 (2.48)	1.48 (-5.22, 8.18)
	Treatment P-value			0.66405
	Hedge's g (95% CI)			0.10 (-0.43, 0.64)

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.EF.MM.S4.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Emotional Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Region

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Rest of the World	N, n	132, 114	134, 102	
	Baseline Mean (SD)	77.12 (20.79)	79.90 (18.85)	
	Change from Baseline LS Mean (SE)	1.60 (1.12)	0.01 (1.20)	1.59 (-1.64, 4.81)
	Treatment P-value			0.33360
	Hedge's g (95% CI)			0.10 (-0.16, 0.37)
	Interaction P-value [b]			0.06120

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.EF.MM.S5.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Emotional Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
0	N, n	120, 102	124, 92	
	Baseline Mean (SD)	82.43 (18.01)	79.53 (19.39)	
	Change from Baseline LS Mean (SE)	0.66 (1.17)	0.96 (1.24)	-0.30 (-3.65, 3.05)
	Treatment P-value			0.86115
	Hedge's g (95% CI)			-0.02 (-0.30, 0.26)
1	N, n	181, 130	183, 104	
	Baseline Mean (SD)	74.04 (22.17)	75.96 (21.14)	
	Change from Baseline LS Mean (SE)	2.52 (1.07)	-3.19 (1.20)	5.71 (2.55, 8.87)
	Treatment P-value			0.00042
	Hedge's g (95% CI)			0.34 (0.08, 0.59)
	Interaction P-value [b]			0.14263

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.EF.MM.S6.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Emotional Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Yes	N, n	93, 63	95, 52	
	Baseline Mean (SD)	72.75 (22.46)	79.97 (19.05)	
	Change from Baseline LS Mean (SE)	4.57 (1.53)	-4.41 (1.73)	8.97 (4.44, 13.51)
	Treatment P-value			0.00012
	Hedge's g (95% CI)			0.54 (0.17, 0.91)
No	N, n	208, 169	212, 144	
	Baseline Mean (SD)	79.59 (19.94)	76.79 (20.82)	
	Change from Baseline LS Mean (SE)	0.61 (0.94)	-0.15 (1.02)	0.76 (-1.97, 3.49)
	Treatment P-value			0.58376
	Hedge's g (95% CI)			0.05 (-0.17, 0.27)
	Interaction P-value [b]			0.48972

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.EF.MM.S7.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Emotional Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Paclitaxel	N, n	141, 115	112, 72	
	Baseline Mean (SD)	75.65 (21.75)	78.12 (20.14)	
	Change from Baseline LS Mean (SE)	2.58 (1.11)	1.78 (1.41)	0.80 (-2.72, 4.33)
	Treatment P-value			0.65395
	Hedge's g (95% CI)			0.05 (-0.24, 0.34)
Docetaxel	N, n	87, 65	117, 77	
	Baseline Mean (SD)	80.90 (18.85)	80.52 (17.29)	
	Change from Baseline LS Mean (SE)	-1.40 (1.48)	-2.39 (1.39)	0.99 (-3.00, 4.97)
	Treatment P-value			0.62670
	Hedge's g (95% CI)			0.07 (-0.26, 0.40)

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.EF.MM.S7.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Emotional Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Vinflunine	N, n	73, 52	78, 47	
	Baseline Mean (SD)	78.37 (20.96)	72.16 (24.34)	
	Change from Baseline LS Mean (SE)	3.46 (1.70)	-3.95 (1.78)	7.41 (2.57, 12.24)
	Treatment P-value			0.00274
	Hedge's g (95% CI)			0.44 (0.04, 0.83)
	Interaction P-value [b]			0.01545

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.EF.MM.S8.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Emotional Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Primary Site of Tumor

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Upper Tract	N, n	98, 75	107, 76	
	Baseline Mean (SD)	75.67 (21.30)	75.88 (20.66)	
	Change from Baseline LS Mean (SE)	1.61 (1.39)	0.64 (1.39)	0.97 (-2.89, 4.84)
	Treatment P-value			0.62077
	Hedge's g (95% CI)			0.06 (-0.26, 0.37)
Other	N, n	203, 157	200, 120	
	Baseline Mean (SD)	78.72 (20.59)	78.75 (20.18)	
	Change from Baseline LS Mean (SE)	1.62 (0.98)	-2.43 (1.13)	4.05 (1.12, 6.98)
	Treatment P-value			0.00689
	Hedge's g (95% CI)			0.27 (0.03, 0.51)
	Interaction P-value [b]			0.23133

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.EF.MM.S9.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Emotional Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
1-2 lines	N, n	262, 203	270, 169	
	Baseline Mean (SD)	77.05 (21.12)	77.76 (20.51)	
	Change from Baseline LS Mean (SE)	1.83 (0.87)	-1.76 (0.95)	3.59 (1.07, 6.12)
	Treatment P-value			0.00542
	Hedge's g (95% CI)			0.22 (0.02, 0.43)
>=3 lines	N, n	39, 29	37, 27	
	Baseline Mean (SD)	82.47 (18.28)	76.85 (19.79)	
	Change from Baseline LS Mean (SE)	0.54 (2.14)	2.30 (2.35)	-1.77 (-8.02, 4.49)
	Treatment P-value			0.57893
	Hedge's g (95% CI)			-0.12 (-0.64, 0.39)
	Interaction P-value [b]			0.66829

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.EF.MM.S10.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Emotional Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Best Response to Prior CPI

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Responder	N, n	61, 49	50, 34	
	Baseline Mean (SD)	79.93 (16.83)	75.74 (23.42)	
	Change from Baseline LS Mean (SE)	-1.43 (1.68)	2.73 (2.06)	-4.16 (-9.39, 1.08)
	Treatment P-value			0.11941
	Hedge's g (95% CI)			-0.25 (-0.69, 0.18)
Non-responder	N, n	207, 156	215, 136	
	Baseline Mean (SD)	76.82 (21.45)	77.45 (20.16)	
	Change from Baseline LS Mean (SE)	2.57 (0.97)	-1.61 (1.06)	4.18 (1.35, 7.00)
	Treatment P-value			0.00387
	Hedge's g (95% CI)			0.27 (0.04, 0.50)
	Interaction P-value [b]			0.09163

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

3.1.3.5 Kognitive Funktion

Astellas: 7465-CL-0301
Table EORTC.CF.MM.S1.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Cognitive Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Age Group 1

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
<65 years	N, n	108, 85	111, 68	
	Baseline Mean (SD)	86.86 (16.49)	84.80 (17.92)	
	Change from Baseline LS Mean (SE)	-0.88 (1.34)	-0.54 (1.48)	-0.34 (-4.27, 3.59)
	Treatment P-value			0.86440
	Hedge's g (95% CI)			-0.02 (-0.34, 0.29)
>=65 years	N, n	193, 147	196, 128	
	Baseline Mean (SD)	85.71 (17.77)	85.94 (19.67)	
	Change from Baseline LS Mean (SE)	-2.86 (1.03)	-4.12 (1.12)	1.26 (-1.72, 4.24)
	Treatment P-value			0.40799
	Hedge's g (95% CI)			0.08 (-0.16, 0.31)
	Interaction P-value [b]			0.57227

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.CF.MM.S2.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Cognitive Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Age Group 2

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
<75 years	N, n	249, 195	239, 150	
	Baseline Mean (SD)	86.67 (16.89)	86.44 (17.84)	
	Change from Baseline LS Mean (SE)	-1.96 (0.89)	-1.77 (1.02)	-0.19 (-2.85, 2.46)
	Treatment P-value			0.88688
	Hedge's g (95% CI)			-0.01 (-0.22, 0.20)
>=75 years	N, n	52, 37	68, 46	
	Baseline Mean (SD)	83.33 (19.25)	82.61 (22.49)	
	Change from Baseline LS Mean (SE)	-3.13 (2.06)	-6.41 (1.84)	3.28 (-2.16, 8.71)
	Treatment P-value			0.23633
	Hedge's g (95% CI)			0.19 (-0.24, 0.62)
	Interaction P-value [b]			0.08948

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.CF.MM.S3.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Cognitive Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Gender

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Male	N, n	238, 182	232, 150	
	Baseline Mean (SD)	86.54 (17.71)	86.00 (19.60)	
	Change from Baseline LS Mean (SE)	-2.40 (0.93)	-2.73 (1.03)	0.33 (-2.40, 3.06)
	Treatment P-value			0.81045
	Hedge's g (95% CI)			0.02 (-0.20, 0.24)
Female	N, n	63, 50	75, 46	
	Baseline Mean (SD)	84.67 (15.74)	84.06 (17.20)	
	Change from Baseline LS Mean (SE)	-1.20 (1.76)	-3.16 (1.85)	1.96 (-3.06, 6.98)
	Treatment P-value			0.44248
	Hedge's g (95% CI)			0.14 (-0.26, 0.53)
	Interaction P-value [b]			0.40614

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.CF.MM.S4.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Cognitive Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Region

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Western Europe	N, n	126, 90	129, 70	
	Baseline Mean (SD)	87.22 (15.41)	82.38 (21.96)	
	Change from Baseline LS Mean (SE)	-1.57 (1.31)	-3.25 (1.51)	1.68 (-2.26, 5.61)
	Treatment P-value			0.40245
	Hedge's g (95% CI)			0.10 (-0.21, 0.41)
US	N, n	43, 28	44, 24	
	Baseline Mean (SD)	89.88 (17.18)	83.33 (21.42)	
	Change from Baseline LS Mean (SE)	-0.81 (2.40)	-3.42 (2.54)	2.60 (-4.27, 9.48)
	Treatment P-value			0.45742
	Hedge's g (95% CI)			0.19 (-0.35, 0.72)

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.CF.MM.S4.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Cognitive Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Region

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Rest of the World	N, n	132, 114	134, 102	
	Baseline Mean (SD)	84.36 (18.59)	88.24 (15.84)	
	Change from Baseline LS Mean (SE)	-3.00 (1.16)	-2.40 (1.23)	-0.60 (-3.91, 2.71)
	Treatment P-value			0.72196
	Hedge's g (95% CI)			-0.04 (-0.30, 0.23)
	Interaction P-value [b]			0.06049

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
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Astellas: 7465-CL-0301
Table EORTC.CF.MM.S5.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Cognitive Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
0	N, n	120, 102	124, 92	
	Baseline Mean (SD)	91.99 (14.21)	88.95 (16.07)	
	Change from Baseline LS Mean (SE)	-4.21 (1.20)	-0.94 (1.27)	-3.28 (-6.72, 0.17)
	Treatment P-value			0.06215
	Hedge's g (95% CI)			-0.23 (-0.52, 0.05)
1	N, n	181, 130	183, 104	
	Baseline Mean (SD)	81.54 (18.12)	82.53 (20.95)	
	Change from Baseline LS Mean (SE)	-0.29 (1.09)	-4.51 (1.23)	4.22 (0.99, 7.46)
	Treatment P-value			0.01068
	Hedge's g (95% CI)			0.24 (-0.02, 0.50)
	Interaction P-value [b]			0.01584

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.CF.MM.S6.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Cognitive Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Yes	N, n	93, 63	95, 52	
	Baseline Mean (SD)	83.33 (18.93)	85.58 (15.84)	
	Change from Baseline LS Mean (SE)	-0.54 (1.57)	-4.32 (1.76)	3.79 (-0.85, 8.43)
	Treatment P-value			0.10913
	Hedge's g (95% CI)			0.22 (-0.15, 0.58)
No	N, n	208, 169	212, 144	
	Baseline Mean (SD)	87.18 (16.57)	85.53 (20.12)	
	Change from Baseline LS Mean (SE)	-2.68 (0.96)	-2.33 (1.05)	-0.36 (-3.15, 2.44)
	Treatment P-value			0.80071
	Hedge's g (95% CI)			-0.02 (-0.25, 0.20)
	Interaction P-value [b]			0.69083

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.CF.MM.S7.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Cognitive Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Paclitaxel	N, n	141, 115	112, 72	
	Baseline Mean (SD)	85.65 (16.50)	90.28 (15.76)	
	Change from Baseline LS Mean (SE)	-2.76 (1.16)	-2.75 (1.45)	-0.01 (-3.66, 3.64)
	Treatment P-value			0.99566
	Hedge's g (95% CI)			-0.00 (-0.29, 0.29)
Docetaxel	N, n	87, 65	117, 77	
	Baseline Mean (SD)	87.44 (16.41)	85.71 (16.60)	
	Change from Baseline LS Mean (SE)	-2.80 (1.53)	-3.69 (1.44)	0.89 (-3.25, 5.02)
	Treatment P-value			0.67433
	Hedge's g (95% CI)			0.06 (-0.27, 0.39)

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.CF.MM.S7.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Cognitive Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Vinflunine	N, n	73, 52	78, 47	
	Baseline Mean (SD)	85.58 (20.08)	78.01 (24.60)	
	Change from Baseline LS Mean (SE)	0.32 (1.76)	-1.39 (1.84)	1.71 (-3.30, 6.71)
	Treatment P-value			0.50286
	Hedge's g (95% CI)			0.10 (-0.30, 0.49)
	Interaction P-value [b]			0.24659

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.CF.MM.S8.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Cognitive Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Primary Site of Tumor

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Upper Tract	N, n	98, 75	107, 76	
	Baseline Mean (SD)	83.56 (19.08)	83.99 (21.33)	
	Change from Baseline LS Mean (SE)	-1.95 (1.42)	-2.54 (1.43)	0.59 (-3.37, 4.55)
	Treatment P-value			0.76872
	Hedge's g (95% CI)			0.03 (-0.28, 0.35)
Other	N, n	203, 157	200, 120	
	Baseline Mean (SD)	87.37 (16.28)	86.53 (17.46)	
	Change from Baseline LS Mean (SE)	-2.26 (1.00)	-3.06 (1.15)	0.80 (-2.20, 3.81)
	Treatment P-value			0.59979
	Hedge's g (95% CI)			0.05 (-0.18, 0.29)
	Interaction P-value [b]			0.85652

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.CF.MM.S9.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Cognitive Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
1-2 lines	N, n	262, 203	270, 169	
	Baseline Mean (SD)	85.30 (17.36)	85.11 (19.59)	
	Change from Baseline LS Mean (SE)	-1.68 (0.89)	-2.76 (0.97)	1.08 (-1.51, 3.68)
	Treatment P-value			0.41094
	Hedge's g (95% CI)			0.07 (-0.14, 0.27)
>=3 lines	N, n	39, 29	37, 27	
	Baseline Mean (SD)	91.95 (15.82)	88.27 (15.20)	
	Change from Baseline LS Mean (SE)	-4.88 (2.21)	-3.35 (2.41)	-1.54 (-7.97, 4.89)
	Treatment P-value			0.63895
	Hedge's g (95% CI)			-0.11 (-0.62, 0.41)
	Interaction P-value [b]			0.73387

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.CF.MM.S10.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Cognitive Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Best Response to Prior CPI

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Responder	N, n	61, 49	50, 34	
	Baseline Mean (SD)	86.73 (14.02)	89.71 (13.62)	
	Change from Baseline LS Mean (SE)	-5.24 (1.75)	-4.21 (2.12)	-1.03 (-6.44, 4.38)
	Treatment P-value			0.70770
	Hedge's g (95% CI)			-0.06 (-0.50, 0.37)
Non-responder	N, n	207, 156	215, 136	
	Baseline Mean (SD)	86.00 (18.01)	84.19 (20.52)	
	Change from Baseline LS Mean (SE)	-1.36 (1.01)	-2.59 (1.09)	1.23 (-1.69, 4.15)
	Treatment P-value			0.40638
	Hedge's g (95% CI)			0.08 (-0.15, 0.31)
	Interaction P-value [b]			0.19873

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

3.1.3.6 Soziale Funktion

Astellas: 7465-CL-0301
Table EORTC.SF.MM.S1.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Social Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Age Group 1

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
<65 years	N, n	108, 85	111, 68	
	Baseline Mean (SD)	78.82 (24.99)	79.66 (24.91)	
	Change from Baseline LS Mean (SE)	-4.93 (1.88)	-7.64 (2.09)	2.71 (-2.81, 8.23)
	Treatment P-value			0.33432
	Hedge's g (95% CI)			0.14 (-0.18, 0.46)
>=65 years	N, n	193, 147	196, 128	
	Baseline Mean (SD)	82.43 (23.95)	81.77 (22.57)	
	Change from Baseline LS Mean (SE)	-5.67 (1.43)	-10.66 (1.55)	4.99 (0.84, 9.14)
	Treatment P-value			0.01858
	Hedge's g (95% CI)			0.22 (-0.01, 0.46)
	Interaction P-value [b]			0.35427

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients. Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.SF.MM.S2.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Social Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Age Group 2

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
<75 years	N, n	249, 195	239, 150	
	Baseline Mean (SD)	80.77 (24.45)	80.56 (24.46)	
	Change from Baseline LS Mean (SE)	-5.64 (1.24)	-8.83 (1.42)	3.19 (-0.51, 6.90)
	Treatment P-value			0.09099
	Hedge's g (95% CI)			0.15 (-0.06, 0.37)
>=75 years	N, n	52, 37	68, 46	
	Baseline Mean (SD)	82.88 (24.05)	82.61 (19.55)	
	Change from Baseline LS Mean (SE)	-4.03 (2.91)	-12.14 (2.60)	8.11 (0.44, 15.78)
	Treatment P-value			0.03832
	Hedge's g (95% CI)			0.35 (-0.08, 0.78)
	Interaction P-value [b]			0.30387

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.SF.MM.S3.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Social Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Gender

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Male	N, n	238, 182	232, 150	
	Baseline Mean (SD)	81.78 (23.62)	80.78 (23.23)	
	Change from Baseline LS Mean (SE)	-5.90 (1.29)	-9.17 (1.43)	3.26 (-0.51, 7.04)
	Treatment P-value			0.09019
	Hedge's g (95% CI)			0.15 (-0.07, 0.37)
Female	N, n	63, 50	75, 46	
	Baseline Mean (SD)	78.67 (26.95)	81.88 (24.04)	
	Change from Baseline LS Mean (SE)	-3.47 (2.46)	-10.96 (2.59)	7.50 (0.48, 14.51)
	Treatment P-value			0.03622
	Hedge's g (95% CI)			0.37 (-0.03, 0.77)
	Interaction P-value [b]			0.35877

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.SF.MM.S4.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Social Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Region

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Western Europe	N, n	126, 90	129, 70	
	Baseline Mean (SD)	82.59 (23.02)	76.19 (29.29)	
	Change from Baseline LS Mean (SE)	-5.52 (1.81)	-14.38 (2.09)	8.86 (3.42, 14.29)
	Treatment P-value			0.00146
	Hedge's g (95% CI)			0.38 (0.07, 0.70)
US	N, n	43, 28	44, 24	
	Baseline Mean (SD)	83.93 (22.90)	82.64 (20.55)	
	Change from Baseline LS Mean (SE)	-0.62 (3.32)	-6.42 (3.55)	5.80 (-3.76, 15.35)
	Treatment P-value			0.23380
	Hedge's g (95% CI)			0.27 (-0.27, 0.81)

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.SF.MM.S4.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Social Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Region

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Rest of the World	N, n	132, 114	134, 102	
	Baseline Mean (SD)	79.24 (25.72)	83.99 (18.60)	
	Change from Baseline LS Mean (SE)	-6.41 (1.60)	-7.14 (1.69)	0.74 (-3.83, 5.31)
	Treatment P-value			0.75085
	Hedge's g (95% CI)			0.04 (-0.23, 0.30)
	Interaction P-value [b]			0.02088

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.SF.MM.S5.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Social Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: ECOG PS from IRT Strata

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
0	N, n	120, 102	124, 92	
	Baseline Mean (SD)	89.05 (18.98)	84.78 (21.20)	
	Change from Baseline LS Mean (SE)	-9.59 (1.66)	-5.52 (1.76)	-4.08 (-8.84, 0.68)
	Treatment P-value			0.09307
	Hedge's g (95% CI)			-0.20 (-0.48, 0.08)
1	N, n	181, 130	183, 104	
	Baseline Mean (SD)	74.87 (26.27)	77.72 (24.75)	
	Change from Baseline LS Mean (SE)	-1.73 (1.51)	-13.28 (1.70)	11.55 (7.09, 16.01)
	Treatment P-value			<.00001
	Hedge's g (95% CI)			0.52 (0.26, 0.78)
	Interaction P-value [b]			0.00039

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.SF.MM.S6.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Social Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Liver Metastasis from IRT Strata

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Yes	N, n	93, 63	95, 52	
	Baseline Mean (SD)	77.25 (25.80)	81.09 (21.14)	
	Change from Baseline LS Mean (SE)	-2.40 (2.20)	-9.89 (2.46)	7.49 (1.01, 13.97)
	Treatment P-value			0.02351
	Hedge's g (95% CI)			0.34 (-0.03, 0.70)
No	N, n	208, 169	212, 144	
	Baseline Mean (SD)	82.54 (23.70)	81.02 (24.19)	
	Change from Baseline LS Mean (SE)	-6.43 (1.34)	-9.47 (1.45)	3.05 (-0.83, 6.92)
	Treatment P-value			0.12287
	Hedge's g (95% CI)			0.14 (-0.08, 0.37)
	Interaction P-value [b]			0.79856

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

SOURCE: X:\Numerus\Studies\AST\AST104\Analysis\Prod\Progs\Tab_QOL_MM.SAS
Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.SF.MM.S7.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Social Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Paclitaxel	N, n	141, 115	112, 72	
	Baseline Mean (SD)	79.42 (24.42)	83.80 (22.37)	
	Change from Baseline LS Mean (SE)	-5.00 (1.60)	-7.53 (2.01)	2.53 (-2.51, 7.56)
	Treatment P-value			0.32446
	Hedge's g (95% CI)			0.12 (-0.17, 0.41)
Docetaxel	N, n	87, 65	117, 77	
	Baseline Mean (SD)	85.64 (19.52)	84.20 (19.10)	
	Change from Baseline LS Mean (SE)	-7.28 (2.13)	-9.03 (1.99)	1.76 (-3.97, 7.49)
	Treatment P-value			0.54700
	Hedge's g (95% CI)			0.09 (-0.24, 0.42)

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

SOURCE: X:\Numerus\Studies\AST\AST104\Analysis\Prod\Progs\Tab_QOL_MM.SAS
Date/time of run: 02JUL2021 12:13
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table EORTC.SF.MM.S7.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Social Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Vinflunine	N, n	73, 52	78, 47	
	Baseline Mean (SD)	79.17 (28.94)	71.63 (28.64)	
	Change from Baseline LS Mean (SE)	-3.53 (2.43)	-13.68 (2.55)	10.15 (3.23, 17.07)
	Treatment P-value			0.00415
	Hedge's g (95% CI)			0.43 (0.03, 0.82)
	Interaction P-value [b]			0.06204

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
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Astellas: 7465-CL-0301
Table EORTC.SF.MM.S8.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Social Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Primary Site of Tumor

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Upper Tract	N, n	98, 75	107, 76	
	Baseline Mean (SD)	78.89 (26.75)	81.58 (22.70)	
	Change from Baseline LS Mean (SE)	-4.35 (1.99)	-7.90 (1.99)	3.55 (-1.99, 9.08)
	Treatment P-value			0.20828
	Hedge's g (95% CI)			0.16 (-0.16, 0.48)
Other	N, n	203, 157	200, 120	
	Baseline Mean (SD)	82.17 (23.12)	80.69 (23.87)	
	Change from Baseline LS Mean (SE)	-5.90 (1.39)	-10.67 (1.60)	4.77 (0.60, 8.94)
	Treatment P-value			0.02494
	Hedge's g (95% CI)			0.23 (-0.01, 0.47)
	Interaction P-value [b]			0.54363

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Astellas: 7465-CL-0301
Table EORTC.SF.MM.S9.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Social Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Prior Lines of Systemic Therapy

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
1-2 lines	N, n	262, 203	270, 169	
	Baseline Mean (SD)	80.87 (24.92)	81.07 (23.42)	
	Change from Baseline LS Mean (SE)	-5.60 (1.23)	-9.71 (1.35)	4.12 (0.54, 7.69)
	Treatment P-value			0.02424
	Hedge's g (95% CI)			0.19 (-0.01, 0.40)
>=3 lines	N, n	39, 29	37, 27	
	Baseline Mean (SD)	82.76 (20.16)	80.86 (23.44)	
	Change from Baseline LS Mean (SE)	-4.09 (3.10)	-8.79 (3.38)	4.70 (-4.32, 13.71)
	Treatment P-value			0.30629
	Hedge's g (95% CI)			0.21 (-0.31, 0.73)
	Interaction P-value [b]			0.95659

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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Date/time of run: 02JUL2021 12:13
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Astellas: 7465-CL-0301
Table EORTC.SF.MM.S10.FAS: Mixed Model Repeated Measures (MMRM) Analysis: Change from Baseline - EORTC Social Functioning Score (Week 1 to Week 24) (Full Analysis Set)
Subgroup: Best Response to Prior CPI

Subgroup Level	Statistic	Enfortumab Vedotin	Chemotherapy	Enfortumab Vedotin vs Chemotherapy Mean Difference (95% CI)
Responder	N, n	61, 49	50, 34	
	Baseline Mean (SD)	85.71 (17.68)	78.43 (26.76)	
	Change from Baseline LS Mean (SE)	-10.54 (2.47)	-9.04 (2.99)	-1.50 (-9.13, 6.12)
	Treatment P-value			0.69854
	Hedge's g (95% CI)			-0.06 (-0.50, 0.37)
Non-responder	N, n	207, 156	215, 136	
	Baseline Mean (SD)	78.42 (26.59)	81.00 (22.88)	
	Change from Baseline LS Mean (SE)	-3.81 (1.41)	-10.24 (1.53)	6.43 (2.35, 10.51)
	Treatment P-value			0.00209
	Hedge's g (95% CI)			0.30 (0.07, 0.54)
	Interaction P-value [b]			0.33803

Subgroup analyses are conducted if there exists at least 2 levels with >= 10 patients across treatment arms that have a baseline score and at least one post-baseline score up to Week 24.
N: Number of patients in the subgroup level. n: Number of patients with a baseline and at least one post-baseline score up to Week 24.
Estimates are based on a mixed model which included treatment, baseline PRO, scheduled visit, scheduled visit*baseline PRO and scheduled visit*treatment as fixed effects. Scheduled visit was treated as a repeated measure within patients.
Hedge's g statistic has a bias correction applied.
[a] The Overall analysis included an adjustment for Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[b] Subgroup analysis included an adjustment for subgroup and treatment*subgroup interaction.

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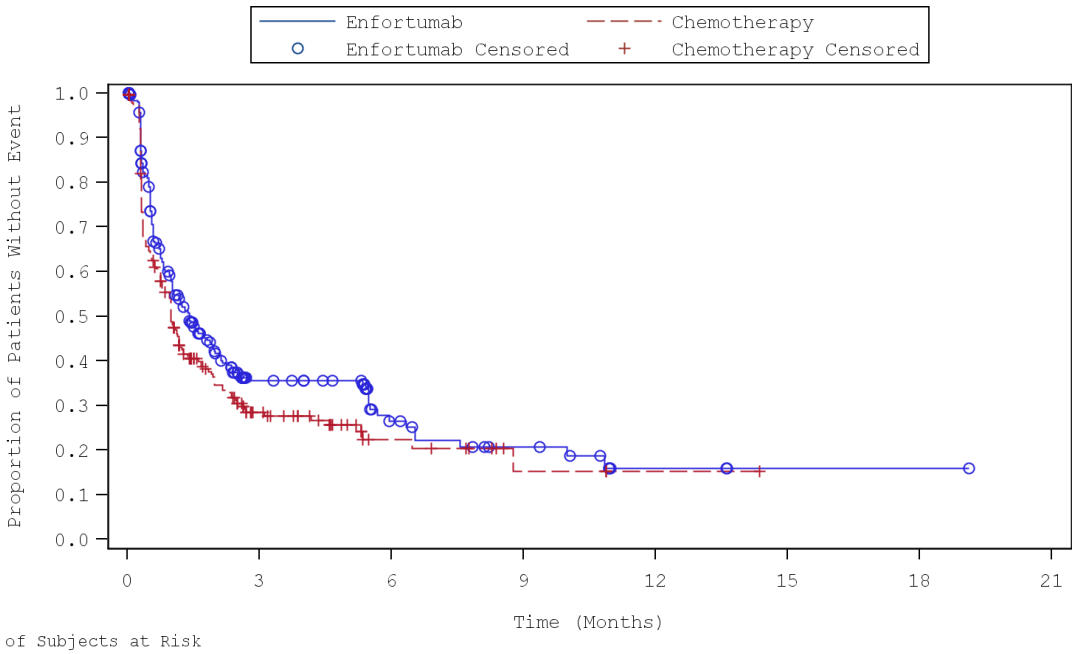
Analysis Plan: 15FEB2021 Confidential

3.2 Kaplan-Meier Kurven zur gesundheitsbezogenen Lebensqualität anhand des EORTC QLQ-C30 – Sensitivitätsanalyse (Responderschwelle ≥ 15 Punkte)

Astellas: 7465-CL-0301
Figure EORTC15.QL.KM.FAS: EORTC Global Health Status: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Overall, Level: NA



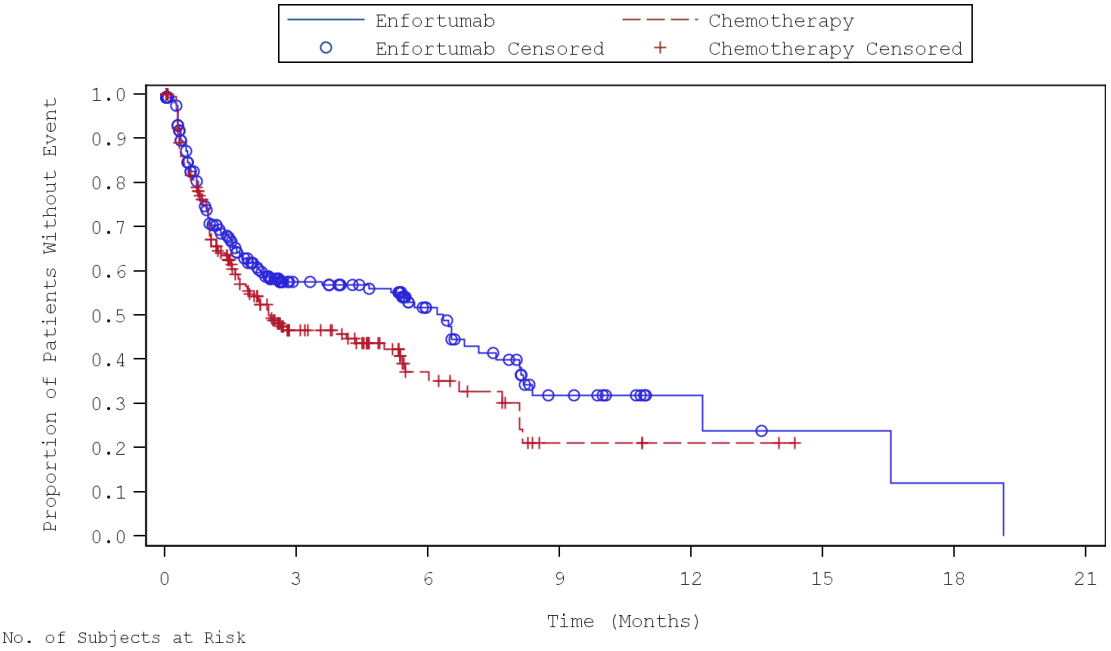
No. of Subjects at Risk

Enfortumab:	301	49	20	11	3	1	1	0
Chemotherapy:	307	36	11	3	1	0	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.793 (0.632, 0.994)
P-value: 0.04555
Enfortumab Median (95% CI): 1.41 (1.02, 1.91)
Chemotherapy Median (95% CI): 0.99 (0.79, 1.18)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_EORTC15_KM_FAS

Astellas: 7465-CL-0301
Figure EORTC15.PF.KM.FAS: EORTC Physical Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Overall, Level: NA



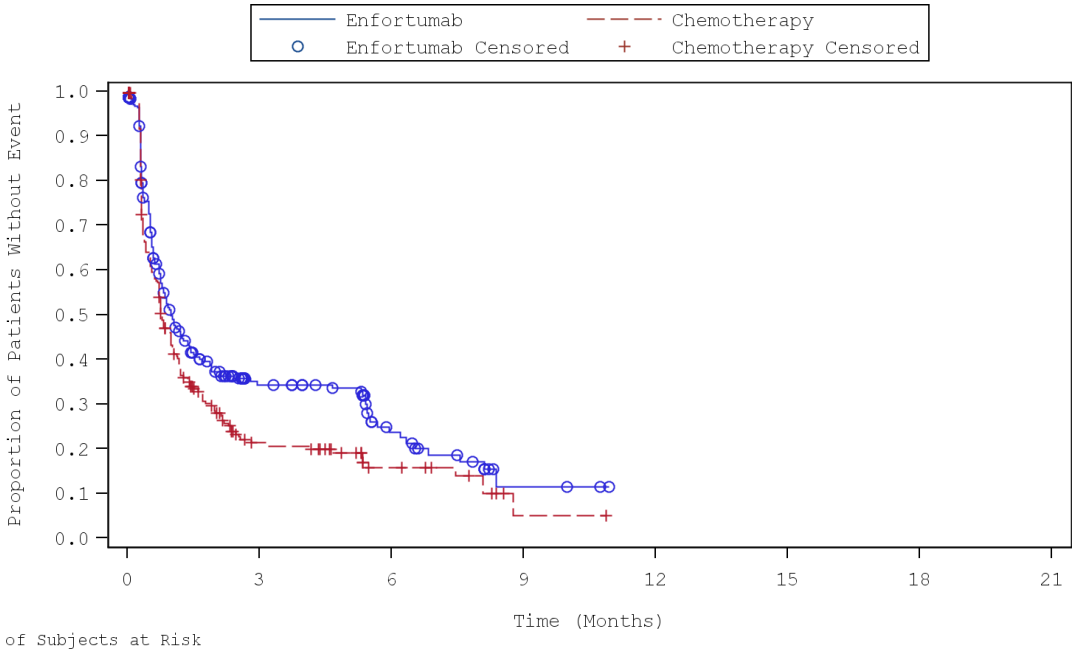
No. of Subjects at Risk

Enfortumab:	301	79	37	12	4	2	1	0
Chemotherapy:	307	56	18	4	2	0	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.776 (0.597, 1.008)
P-value: 0.05775
Enfortumab Median (95% CI): 6.34 (3.58, 7.56)
Chemotherapy Median (95% CI): 2.40 (1.84, 4.99)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_EORTC15_KM_FAS

Astellas: 7465-CL-0301
Figure EORTC15.RF.KM.FAS: EORTC Role Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Overall, Level: NA



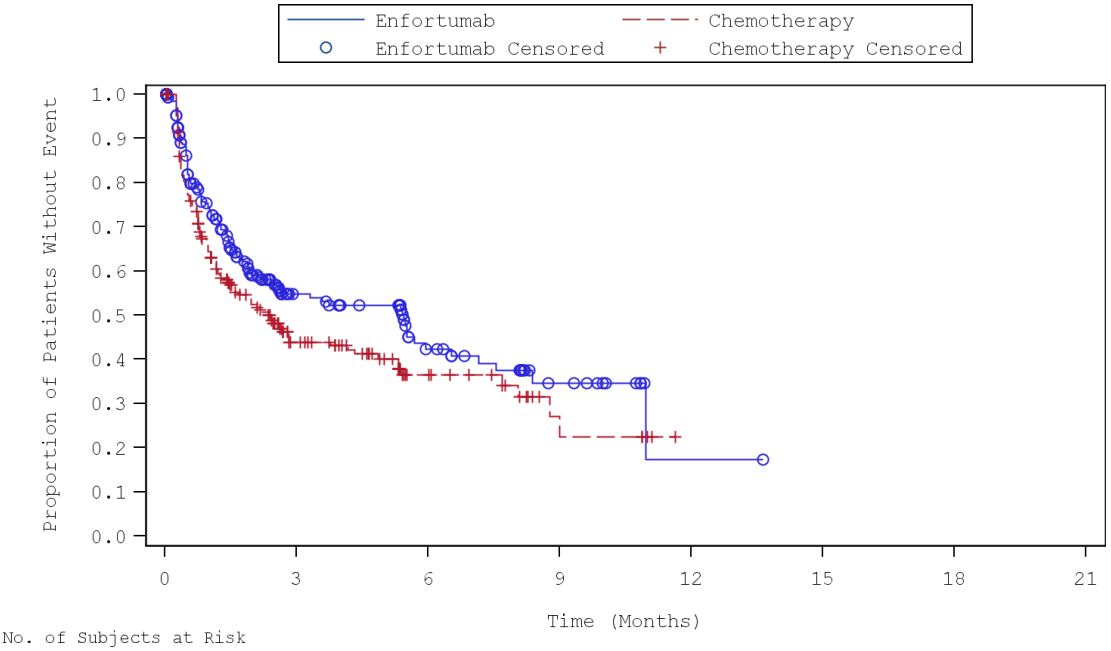
No. of Subjects at Risk

Enfortumab:	301	50	20	3	0	0	0	0
Chemotherapy:	307	31	12	1	0	0	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.764 (0.617, 0.948)
P-value: 0.01474
Enfortumab Median (95% CI): 0.99 (0.79, 1.38)
Chemotherapy Median (95% CI): 0.79 (0.72, 0.99)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_EORTC15_KM_FAS

Astellas: 7465-CL-0301
Figure EORTC15.EF.KM.FAS: EORTC Emotional Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

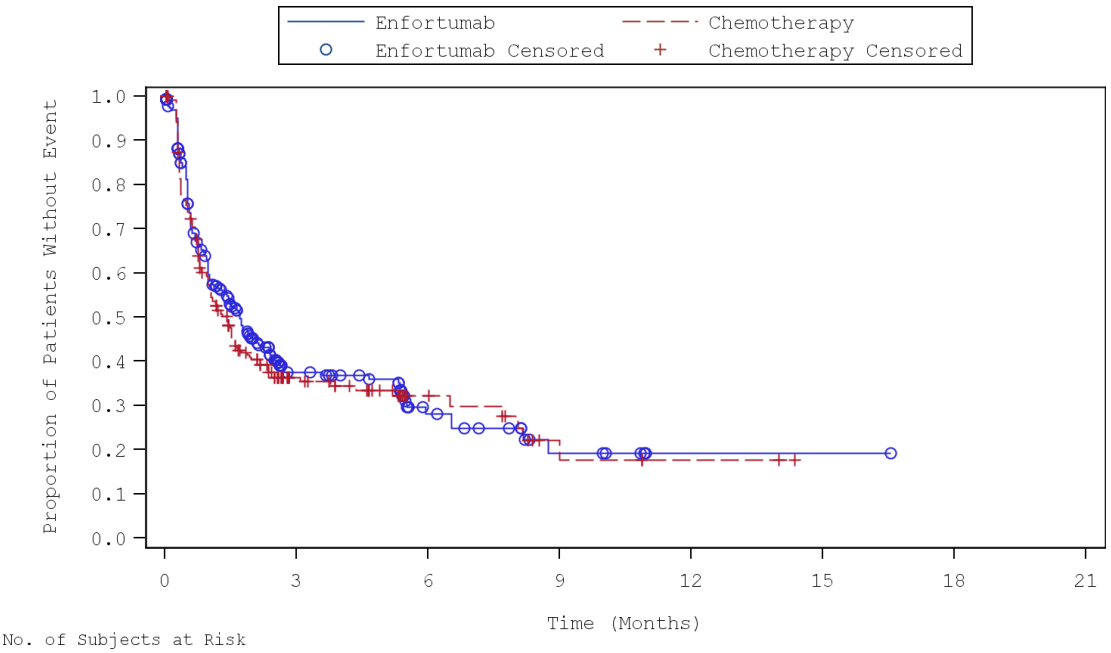
Enfortumab:	301	66	30	11	1	0	0	0
Chemotherapy:	307	57	21	6	0	0	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.732 (0.564, 0.950)
P-value: 0.01878

Enfortumab Median (95% CI): 5.45 (2.46, 6.54)
Chemotherapy Median (95% CI): 2.43 (1.48, 4.17)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_EORTC15_KM_FAS

Astellas: 7465-CL-0301
Figure EORTC15.CF.KM.FAS: EORTC Cognitive Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Overall, Level: NA



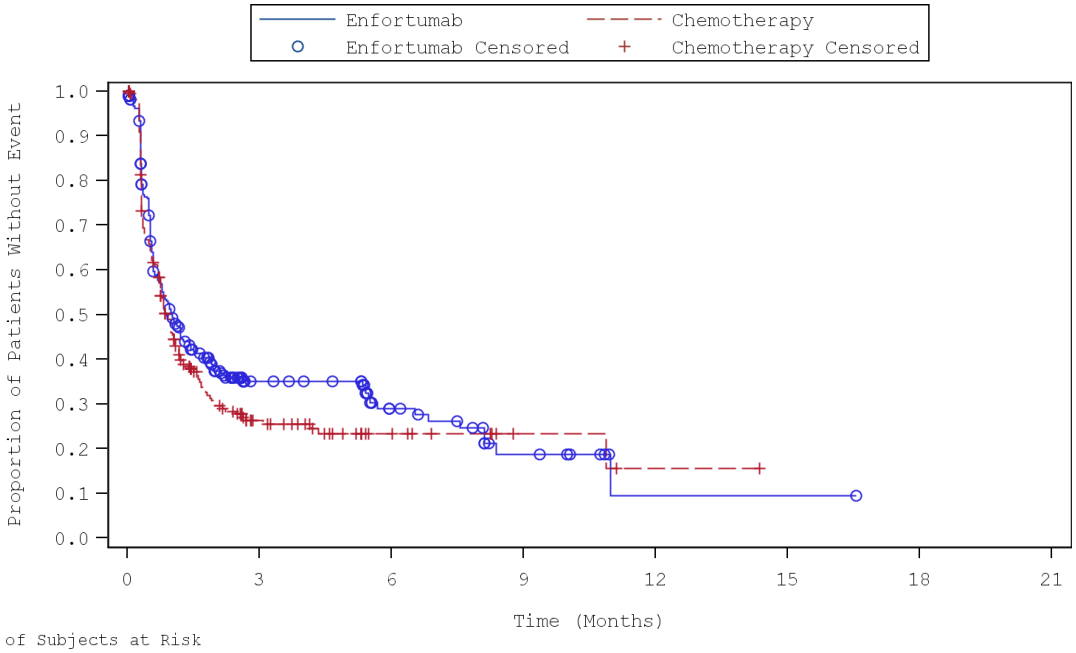
No. of Subjects at Risk

Enfortumab:	301	51	18	6	1	1	0	0
Chemotherapy:	307	41	15	5	2	0	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.905 (0.717, 1.141)
P-value: 0.40115
Enfortumab Median (95% CI): 1.71 (1.28, 2.20)
Chemotherapy Median (95% CI): 1.45 (1.02, 1.64)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_EORTC15_KM_FAS

Astellas: 7465-CL-0301
Figure EORTC15.SF.KM.FAS: EORTC Social Functioning Score: Time to Deterioration of at least 15 points (Months) (Full Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

Enfortumab:	301	46	22	8	1	1	0	0
Chemotherapy:	307	32	11	3	1	0	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.868 (0.694, 1.086)
P-value: 0.20271

Enfortumab Median (95% CI): 1.02 (0.79, 1.41)
Chemotherapy Median (95% CI): 0.89 (0.76, 1.08)

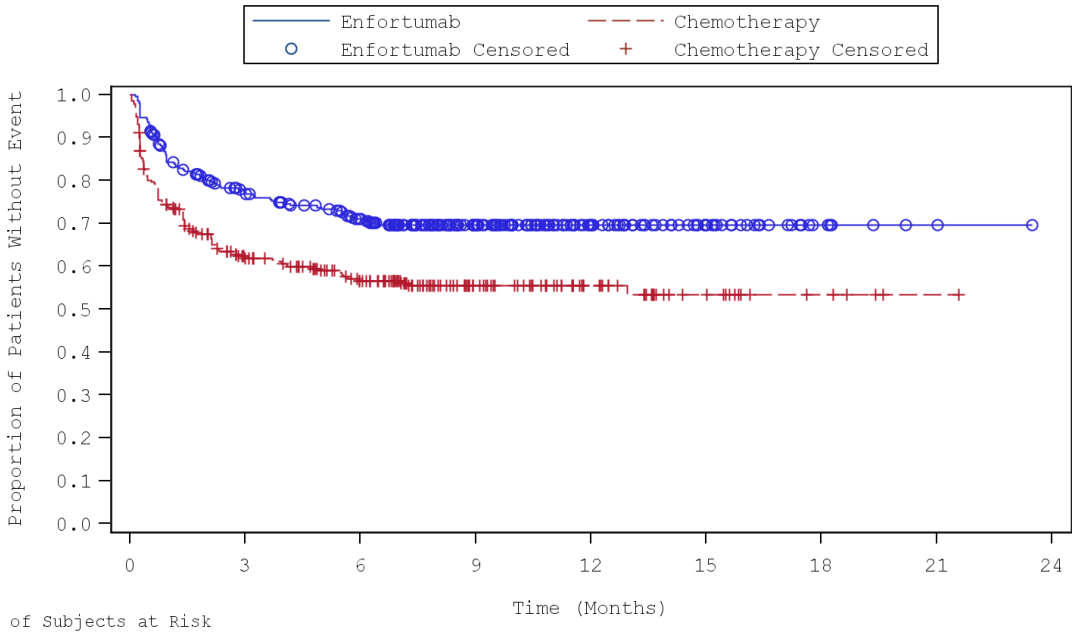
NA: Not Available. NC: Not Calculable.
Reference Table: Tab_EORTC15_KM_FAS

4 Sicherheit

4.1 Kaplan-Meier Kurven zu den SOC und PT der unerwünschten Ereignisse

4.1.1 Gesamtrate

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Blood and lymphatic system disorders (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

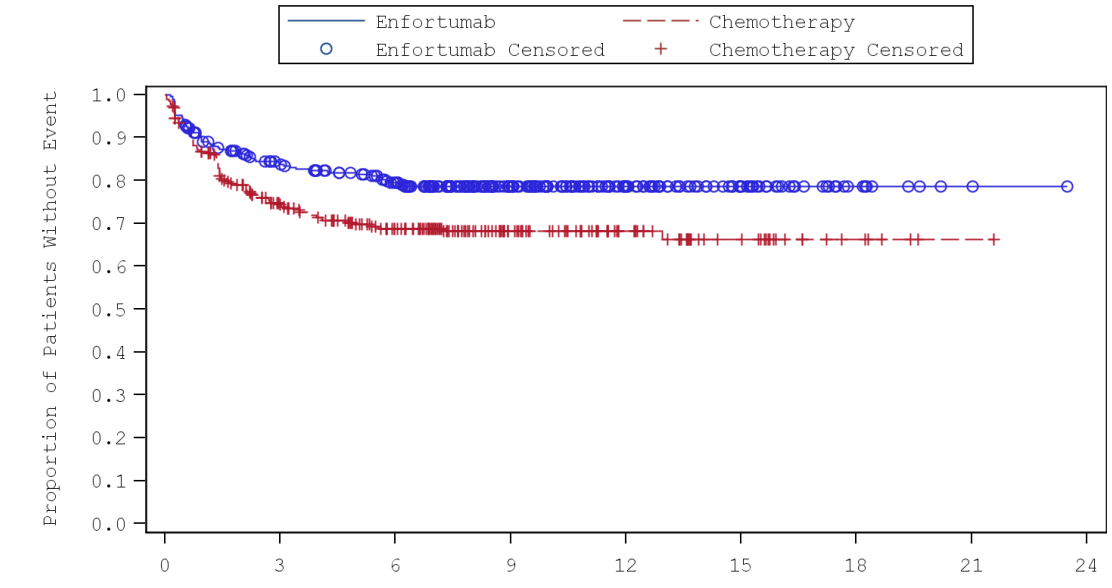
Enfortumab:	296	208	173	104	54	26	7	2	0
Chemotherapy:	291	155	117	62	33	14	5	1	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.586 (0.443, 0.774)
P-value: 0.00014

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (7.06, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Blood and lymphatic system disorders: Anaemia (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

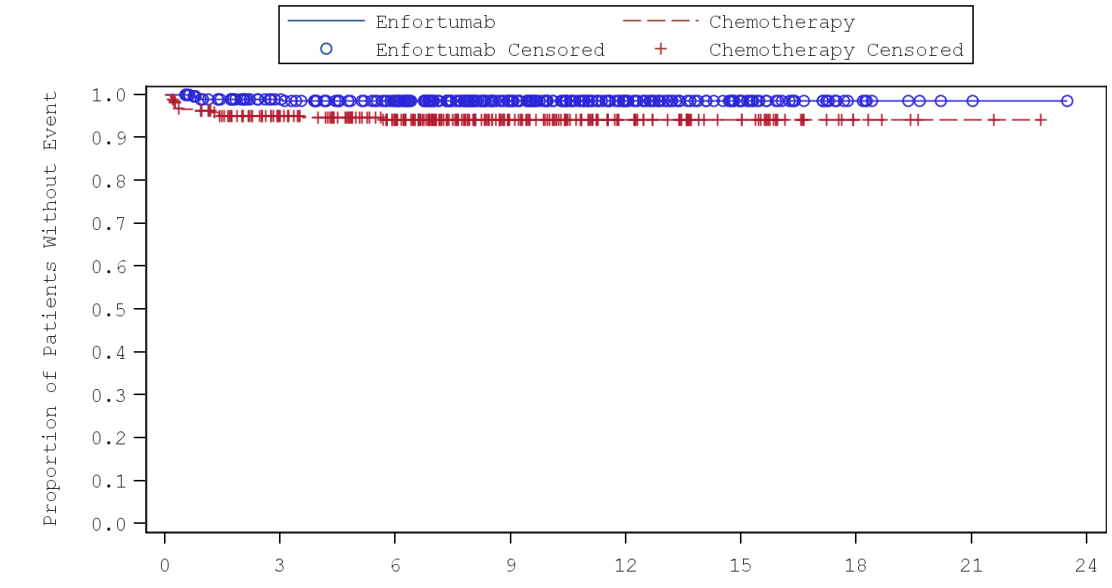
Enfortumab:	296	226	193	117	64	32	9	2	0
Chemotherapy:	291	185	138	76	42	20	6	1	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.626 (0.450, 0.872)
P-value: 0.00529

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Blood and lymphatic system disorders: Febrile neutropenia (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

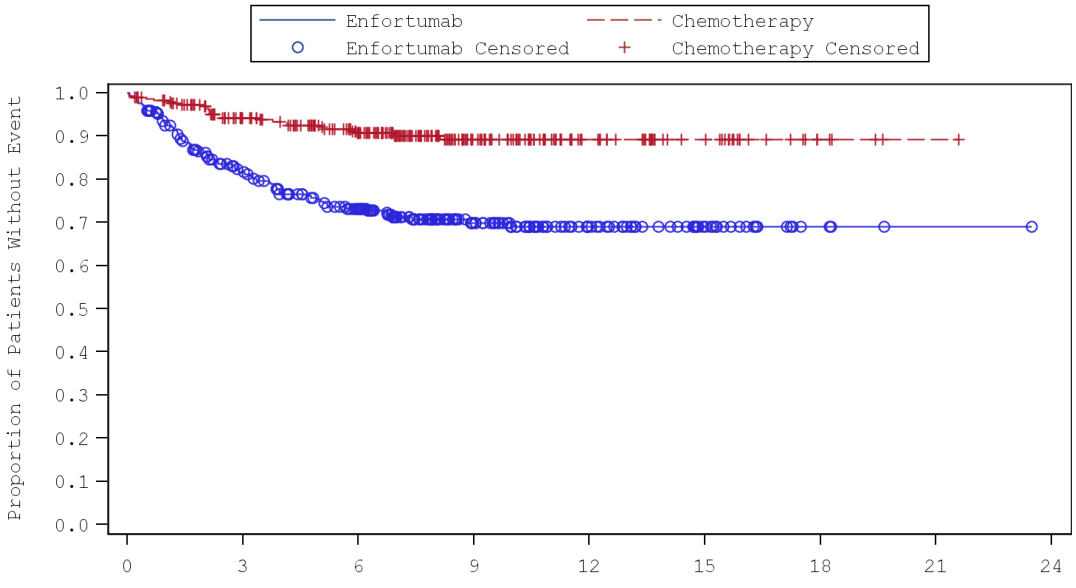
Enfortumab:	296	261	230	141	74	35	9	2	0
Chemotherapy:	291	236	193	103	56	30	6	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.234 (0.078, 0.700)
P-value: 0.00464

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Eye disorders (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

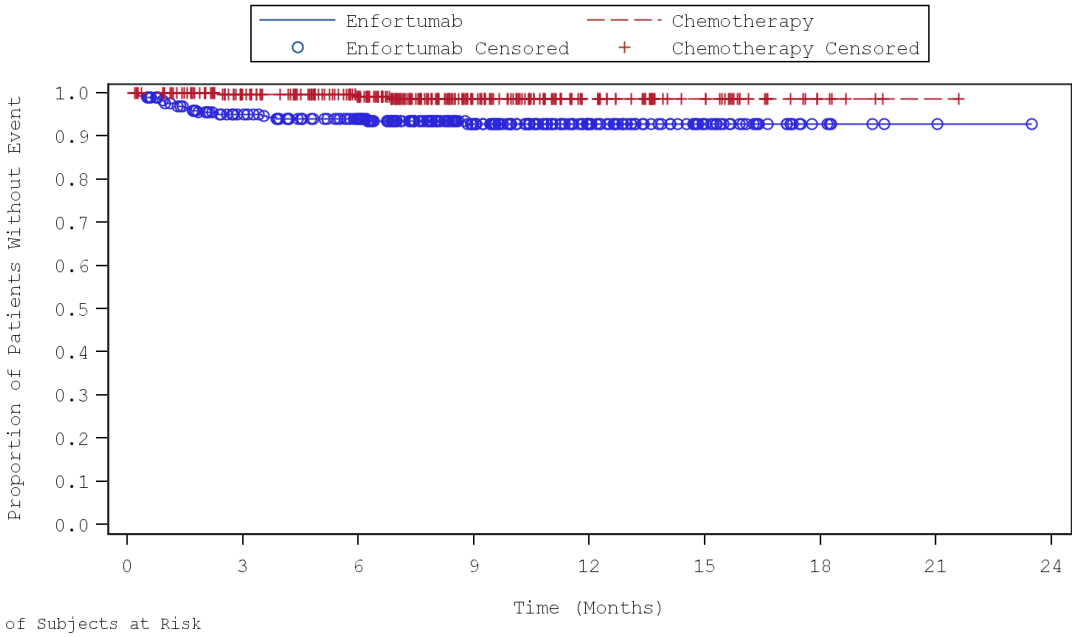
Enfortumab:	296	214	165	89	44	20	4	1	0
Chemotherapy:	291	233	184	92	44	23	5	1	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 3.436 (2.204, 5.356)
P-value: <.00001

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Eye disorders: Dry eye (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

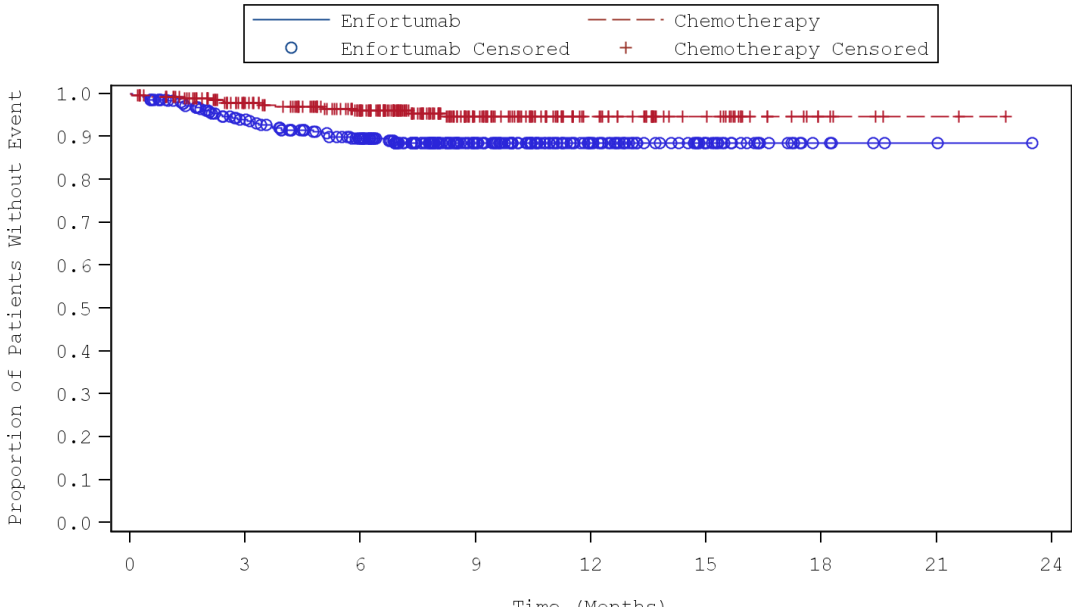
Enfortumab:	296	251	218	131	67	32	7	2	0
Chemotherapy:	291	247	202	106	54	28	6	1	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 6.120 (1.810, 20.696)
P-value: 0.00088

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Eye disorders: Lacrimation increased (Safety Analysis Set)
Subgroup: Overall, Level: NA



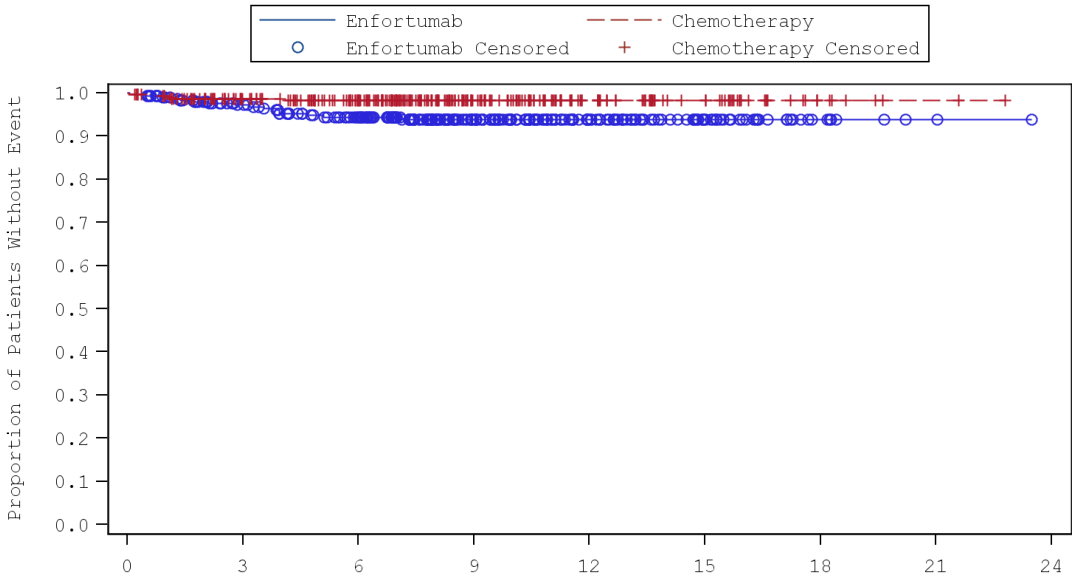
No. of Subjects at Risk									
Enfortumab:	296	246	205	117	60	28	6	2	0
Chemotherapy:	291	242	194	99	50	26	6	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 2.400 (1.226, 4.700)
P-value: 0.00842

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Eye disorders: Vision blurred (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

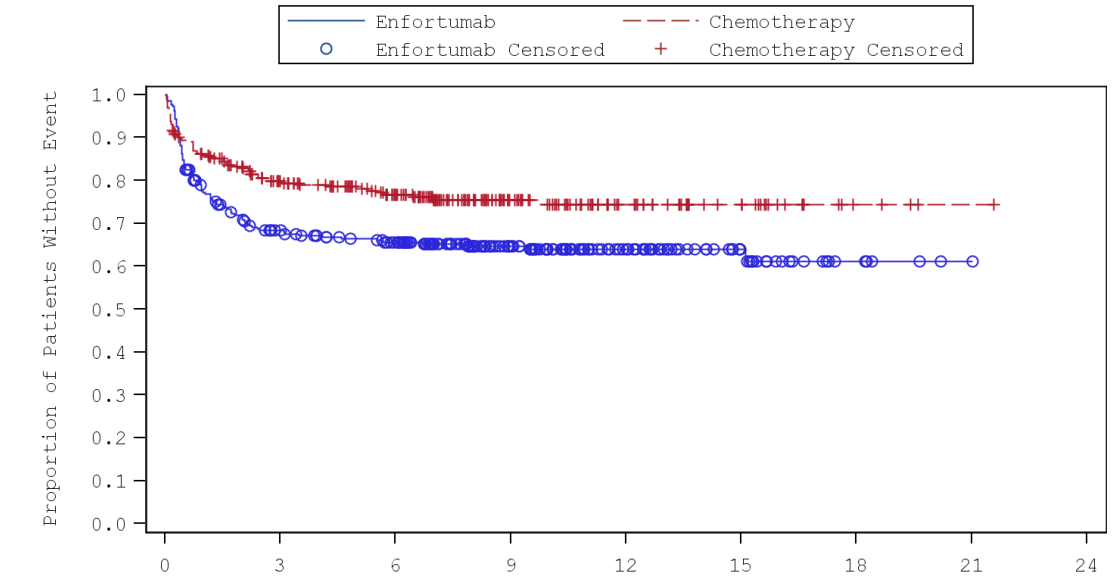
Enfortumab:	296	255	218	129	69	32	8	2	0
Chemotherapy:	291	244	202	107	56	31	7	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 3.199 (1.170, 8.750)
P-value: 0.01668

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Gastrointestinal disorders: Diarrhoea (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

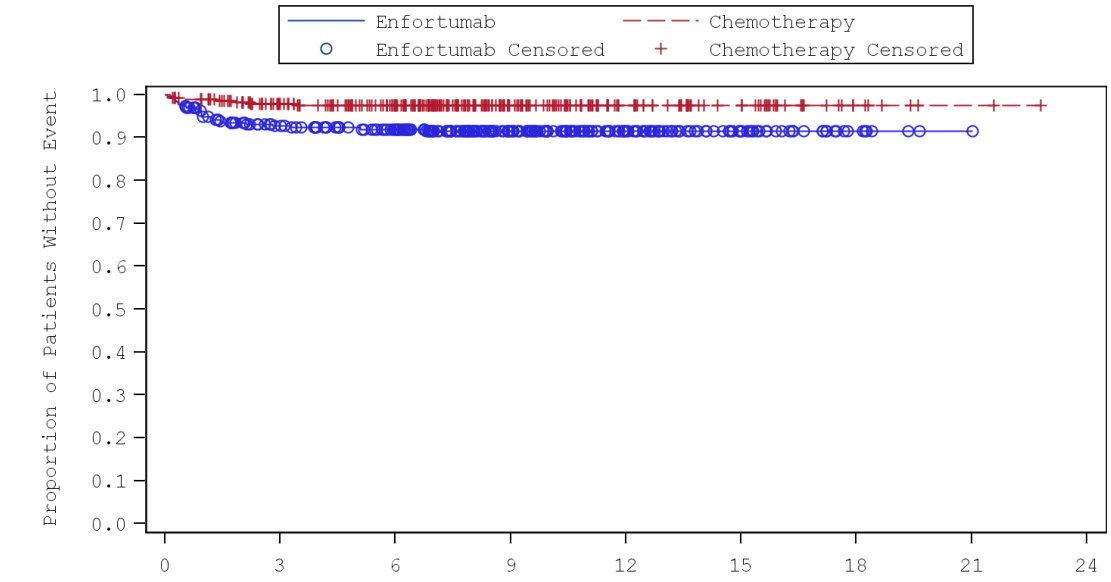
Enfortumab:	296	184	160	96	52	23	6	1	0
Chemotherapy:	291	196	151	75	39	20	4	1	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 1.598 (1.174, 2.177)
P-value: 0.00277

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Gastrointestinal disorders: Dry mouth (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

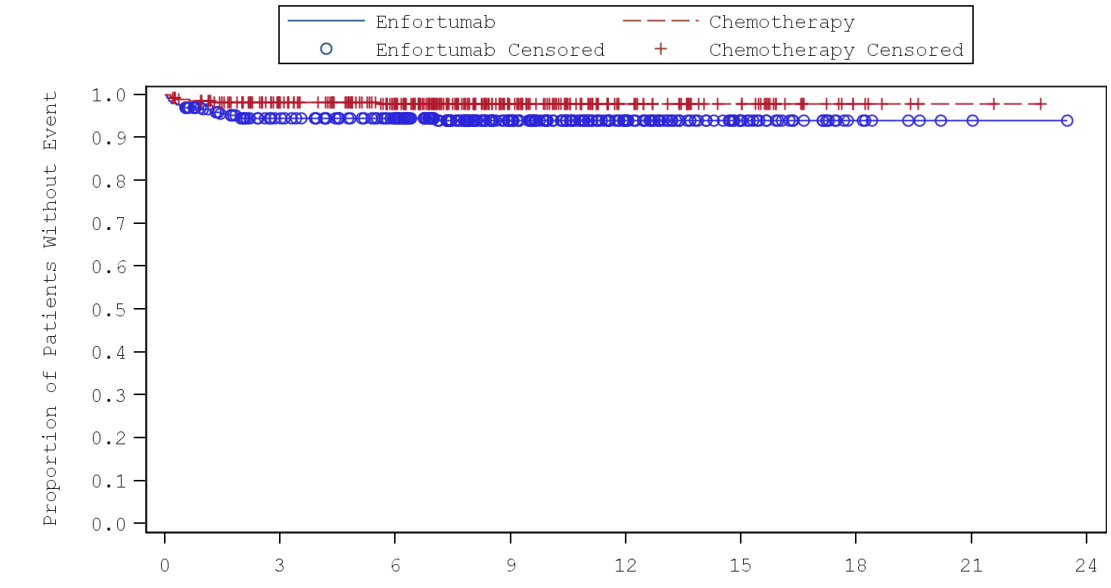
Enfortumab:	296	243	212	127	66	30	7	1	0
Chemotherapy:	291	243	200	106	56	31	7	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 3.251 (1.397, 7.565)
P-value: 0.00393

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - General disorders and administration site conditions: Chills (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

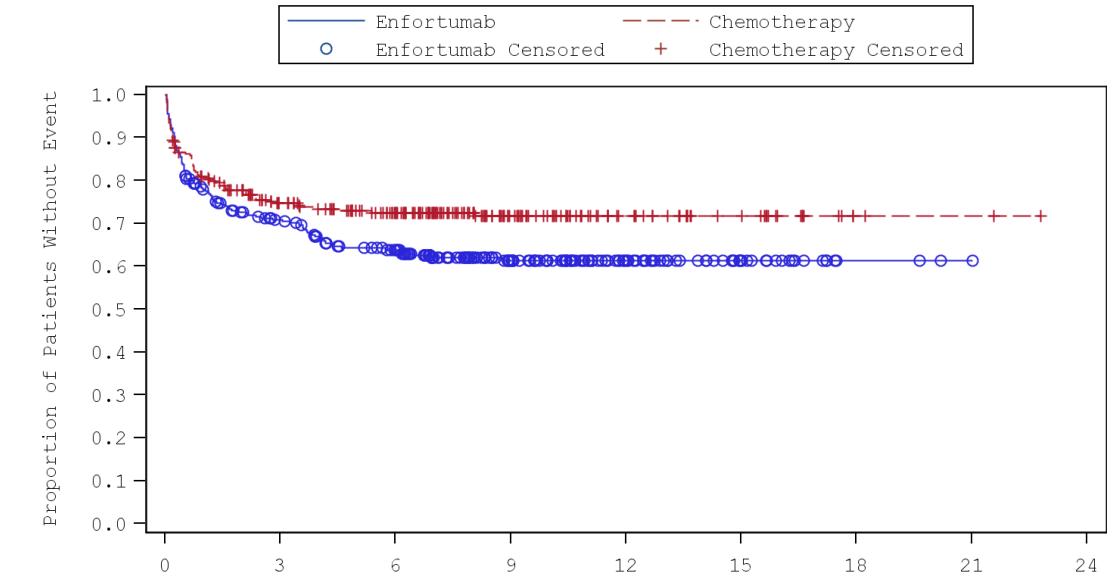
Enfortumab:	296	248	220	132	69	32	8	2	0
Chemotherapy:	291	244	200	105	53	30	7	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 2.657 (1.046, 6.748)
P-value: 0.03256

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - General disorders and administration site conditions: Fatigue (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

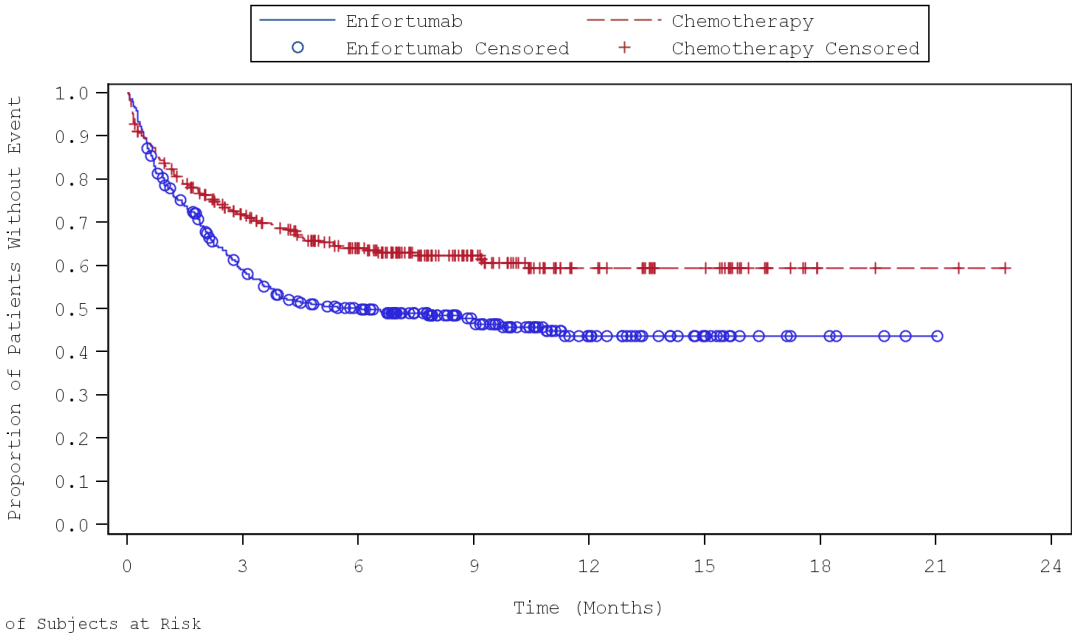
Enfortumab:	296	189	152	87	46	19	3	1	0
Chemotherapy:	291	183	146	71	35	19	3	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 1.376 (1.027, 1.843)
P-value: 0.03176

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Infections and infestations (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

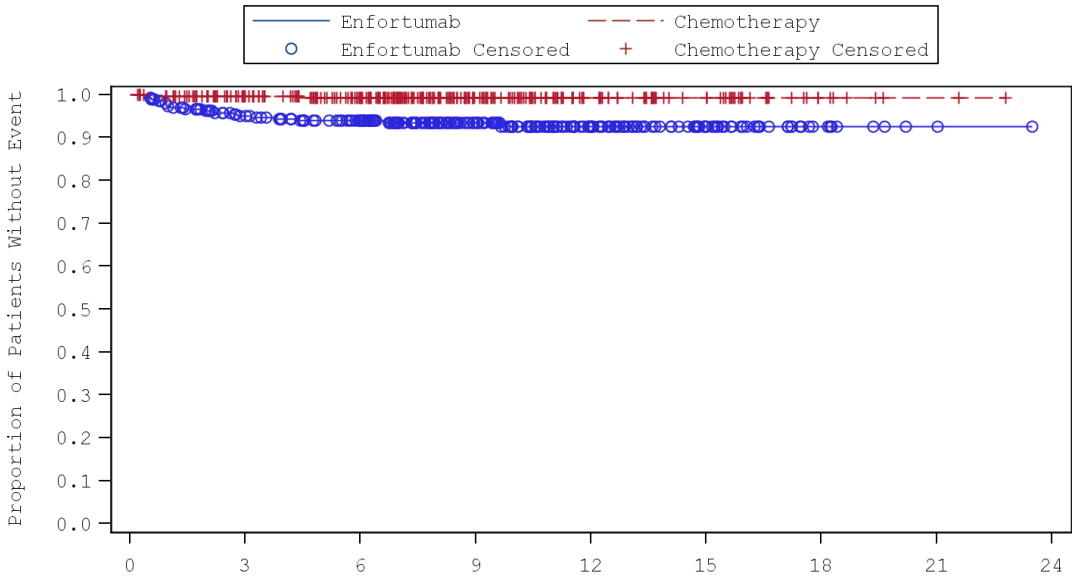
Enfortumab:	296	162	123	75	35	16	5	1	0
Chemotherapy:	291	186	134	71	35	23	3	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 1.473 (1.147, 1.892)
P-value: 0.00231

Enfortumab Median (95% CI): 6.08 (3.52, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Infections and infestations: Conjunctivitis (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

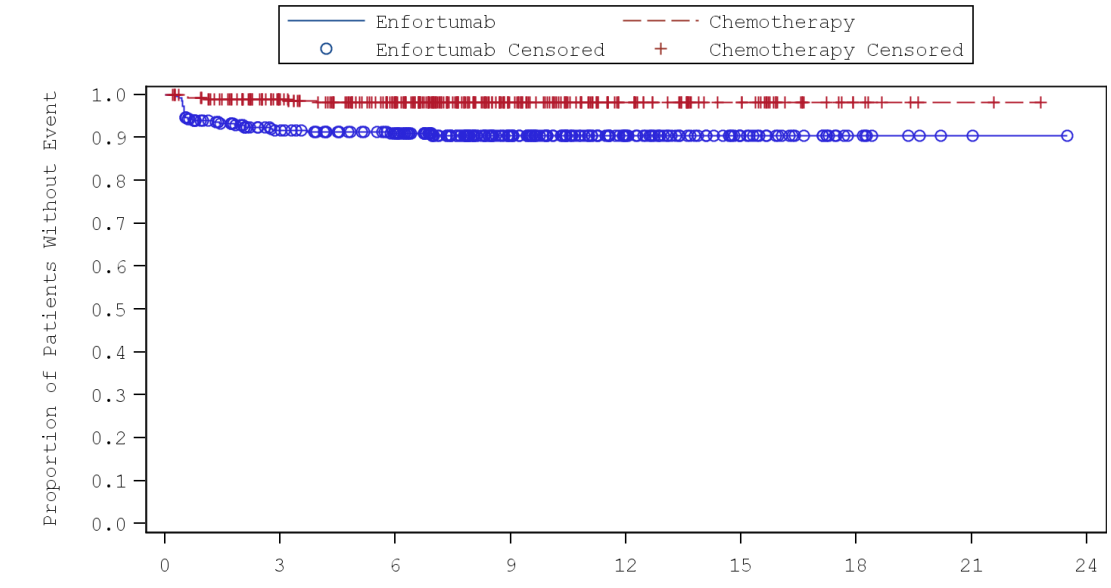
Enfortumab:	296	250	218	135	72	34	9	2	0
Chemotherapy:	291	247	203	109	57	31	7	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 9.898 (2.300, 42.589)
P-value: 0.00015

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Investigations: Alanine aminotransferase increased (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

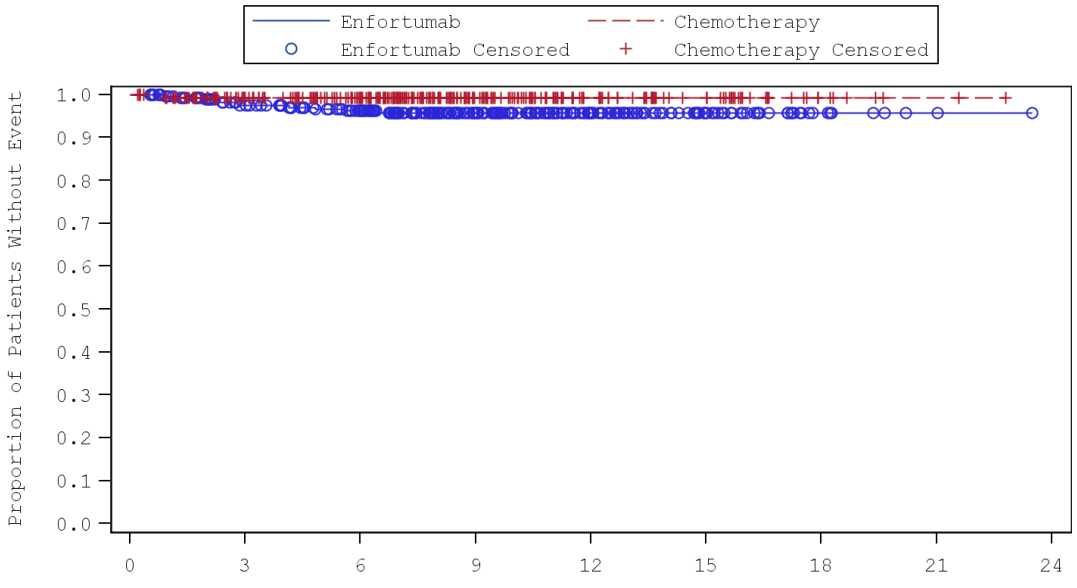
Enfortumab:	296	239	211	127	67	32	9	2	0
Chemotherapy:	291	246	201	107	56	31	7	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 5.272 (2.026, 13.715)
P-value: 0.00014

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Investigations: Amylase increased (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

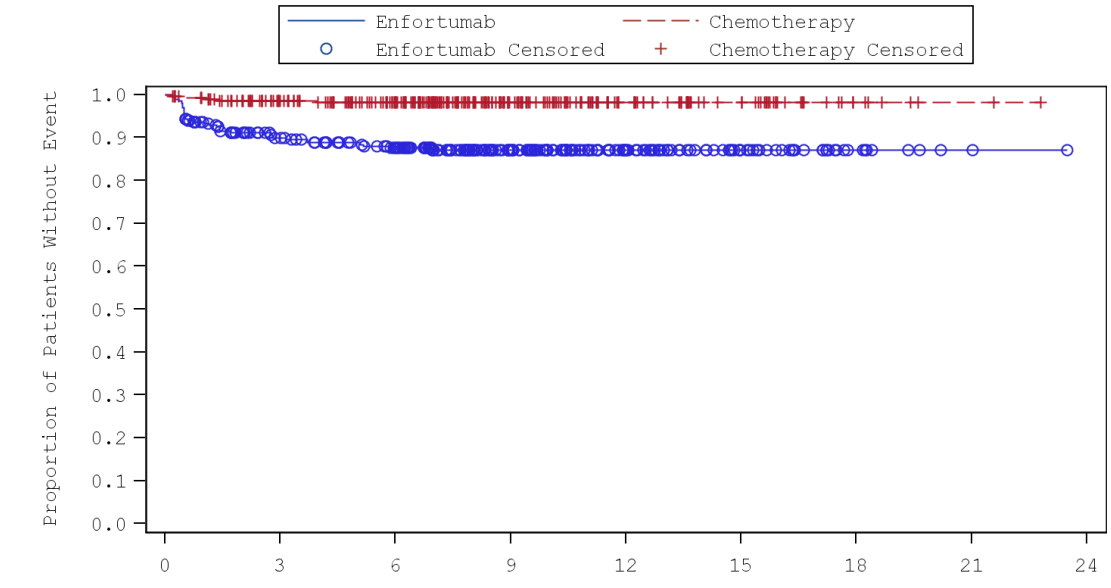
Enfortumab:	296	256	222	137	72	33	8	2	0
Chemotherapy:	291	246	202	108	57	31	7	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 5.466 (1.208, 24.731)
P-value: 0.01332

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Investigations: Aspartate aminotransferase increased (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

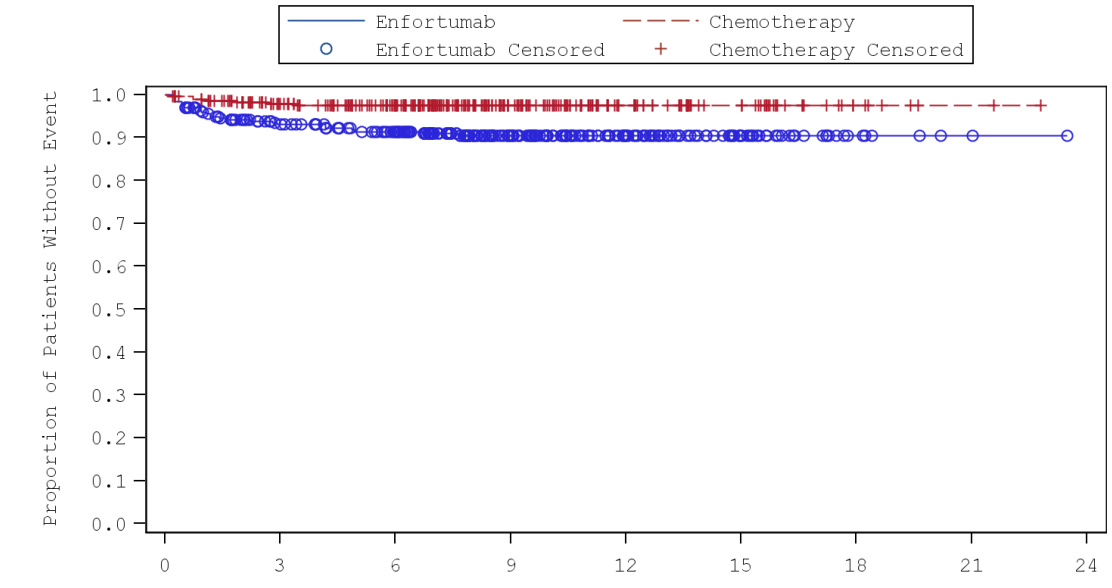
Enfortumab:	296	235	205	124	64	31	9	2	0
Chemotherapy:	291	247	203	108	57	31	7	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 7.237 (2.835, 18.474)
P-value: <.00001

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Investigations: Blood creatinine increased (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

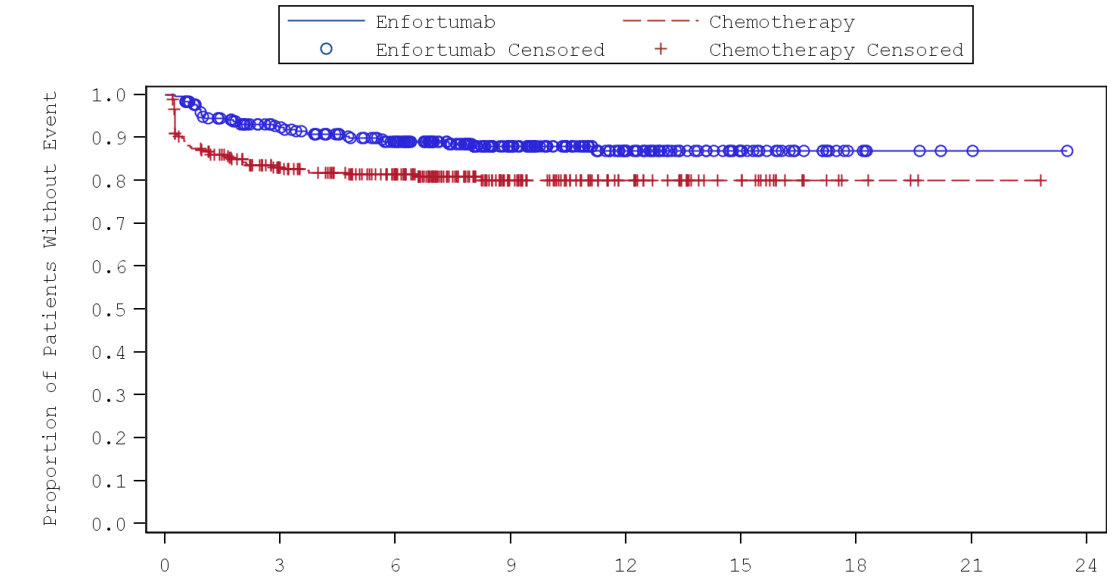
Enfortumab:	296	244	213	127	68	30	7	2	0
Chemotherapy:	291	245	200	107	55	30	7	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 3.902 (1.690, 9.012)
P-value: 0.00059

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Investigations: Neutrophil count decreased (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

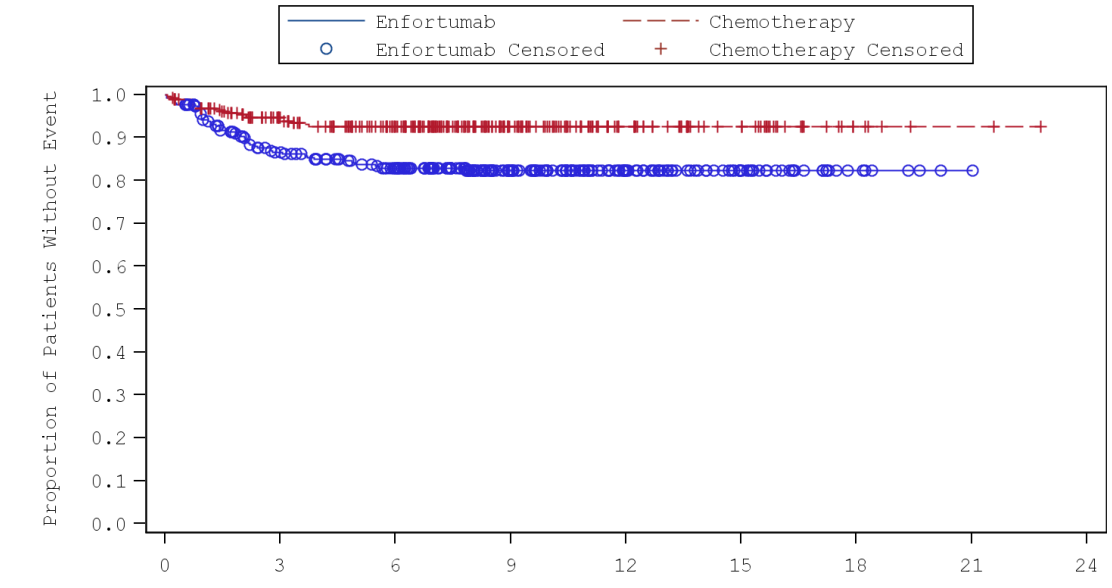
Enfortumab:	296	243	205	123	62	28	7	2	0
Chemotherapy:	291	202	162	81	43	21	4	1	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.507 (0.327, 0.785)
P-value: 0.00215

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Investigations: Weight decreased (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

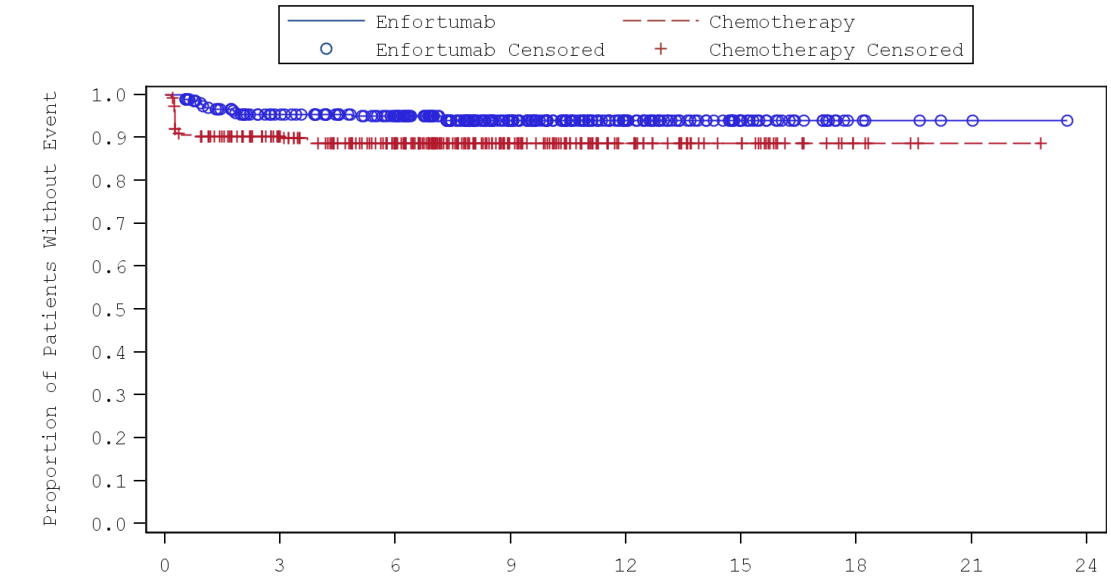
Enfortumab:	296	228	193	115	61	29	7	1	0
Chemotherapy:	291	236	189	100	52	29	6	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 2.357 (1.395, 3.981)
P-value: 0.00097

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Investigations: White blood cell count decreased (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

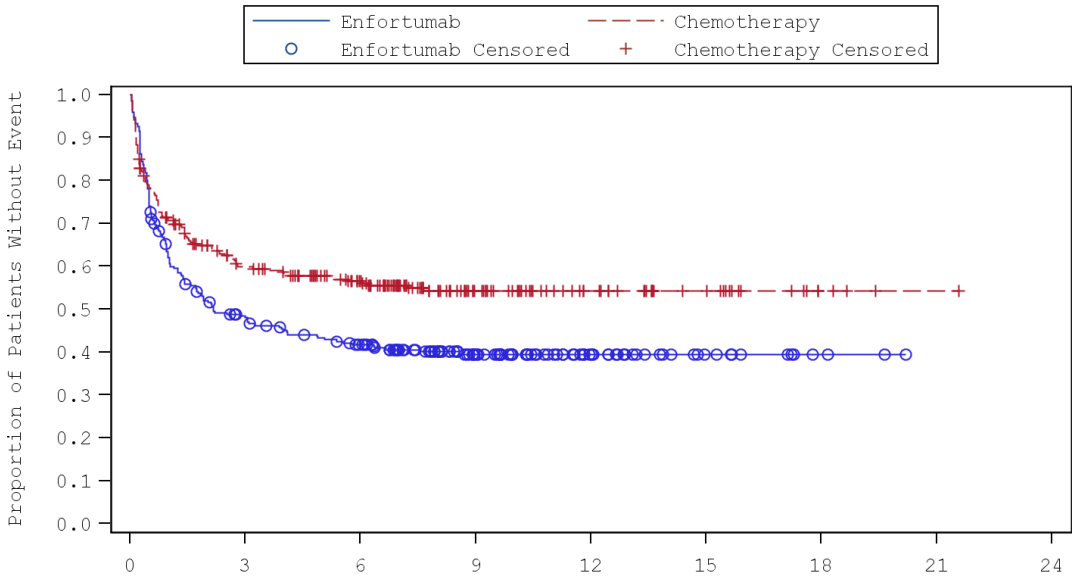
Enfortumab:	296	250	219	131	67	30	6	2	0
Chemotherapy:	291	222	179	94	48	26	5	1	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.449 (0.246, 0.818)
P-value: 0.00791

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Metabolism and nutrition disorders (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

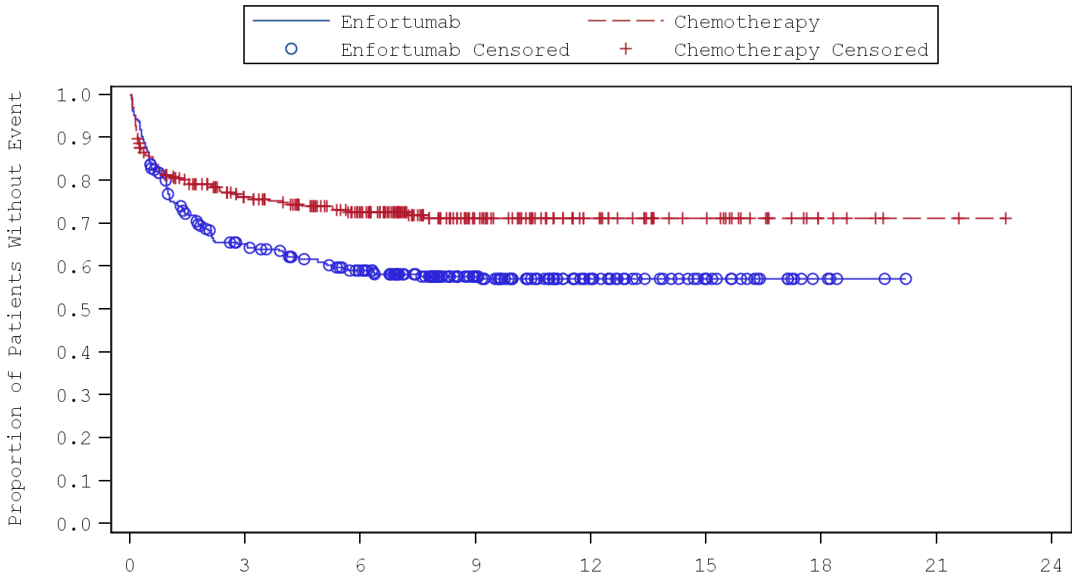
Enfortumab:	296	133	108	59	28	11	3	0	0
Chemotherapy:	291	155	119	57	32	17	4	1	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 1.446 (1.149, 1.821)
P-value: 0.00158

Enfortumab Median (95% CI): 2.17 (1.41, 4.11)
Chemotherapy Median (95% CI): NC (6.05, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Metabolism and nutrition disorders: Decreased appetite (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

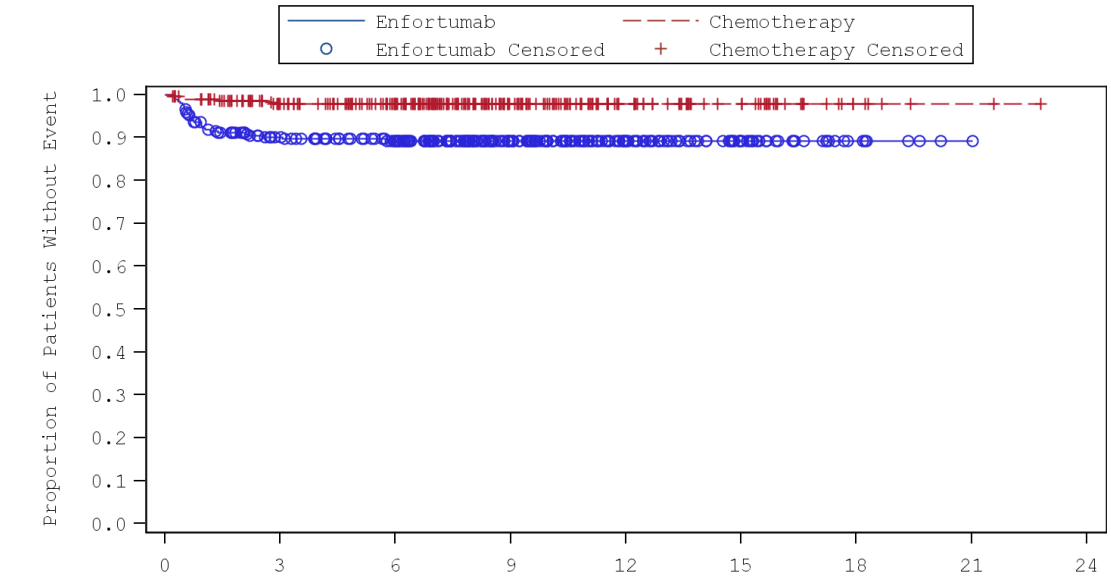
Enfortumab:	296	176	145	88	43	21	5	0	0
Chemotherapy:	291	189	148	75	41	23	6	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 1.542 (1.159, 2.052)
P-value: 0.00262

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Metabolism and nutrition disorders: Hyperglycaemia (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

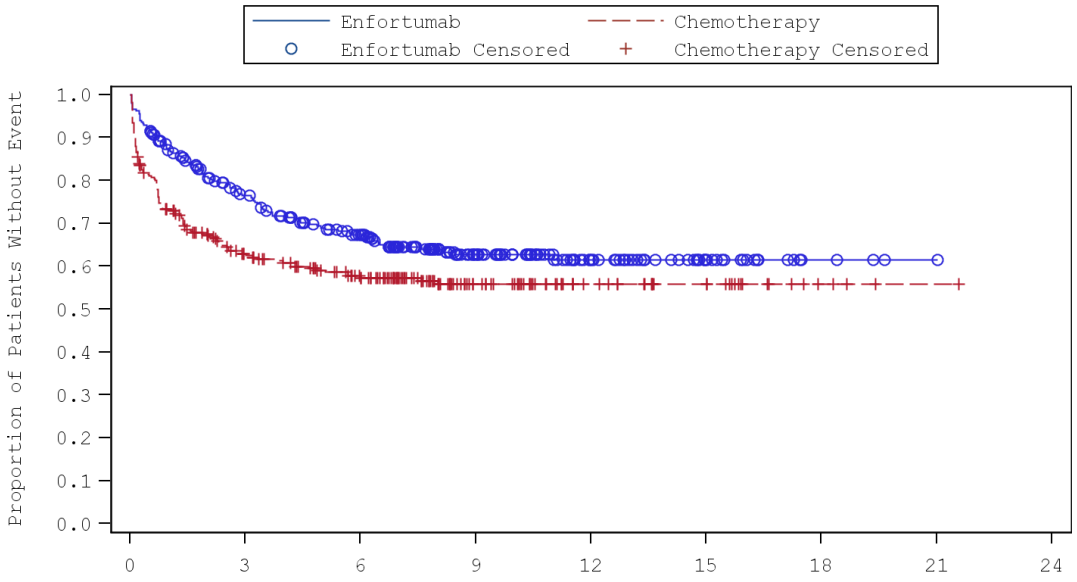
Enfortumab:	296	240	211	126	65	29	7	1	0
Chemotherapy:	291	244	201	106	55	30	6	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 5.134 (2.141, 12.312)
P-value: 0.00004

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Musculoskeletal and connective tissue disorders (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

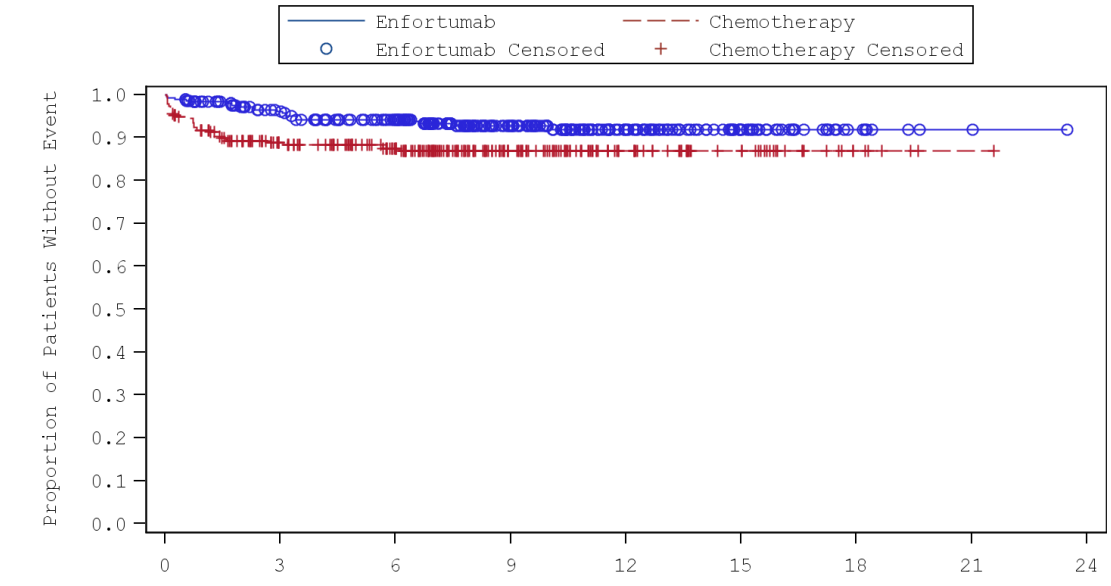
Enfortumab:	296	200	155	85	44	19	4	1	0
Chemotherapy:	291	156	119	57	29	18	4	1	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.682 (0.522, 0.892)
P-value: 0.00531

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (8.02, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Musculoskeletal and connective tissue disorders: Arthralgia (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

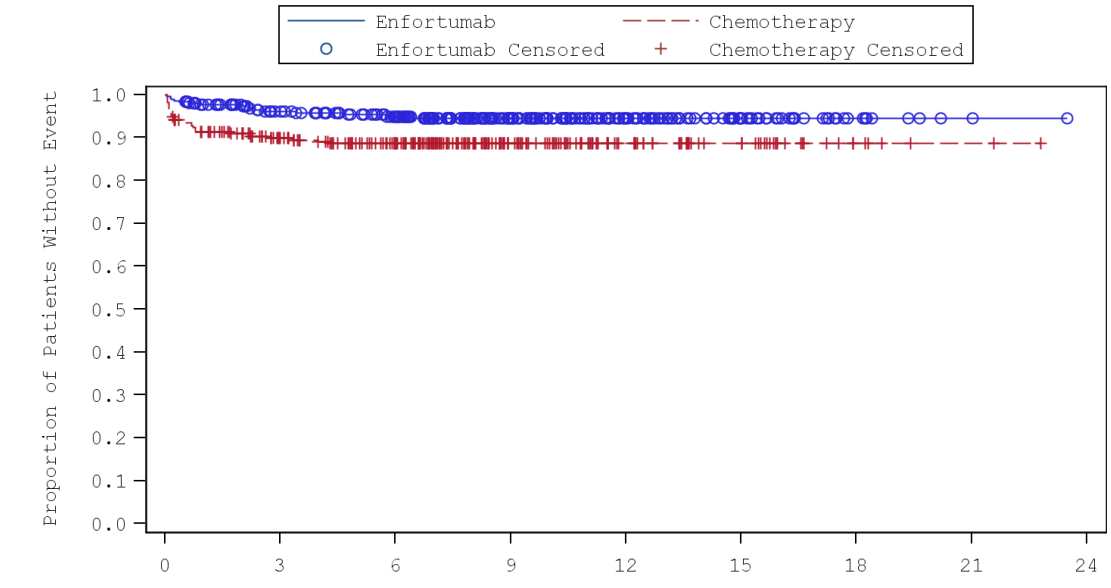
Enfortumab:	296	254	218	130	70	33	8	2	0
Chemotherapy:	291	217	176	96	49	26	6	1	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.479 (0.276, 0.834)
P-value: 0.00785

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Musculoskeletal and connective tissue disorders: Myalgia (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

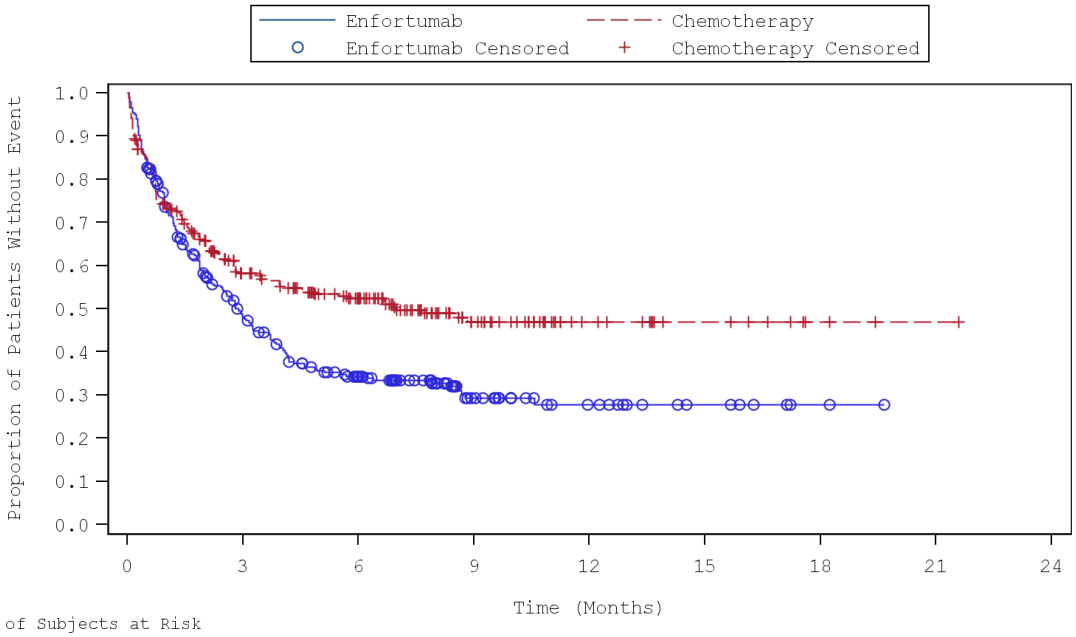
Enfortumab:	296	252	219	131	69	32	9	2	0
Chemotherapy:	291	223	181	94	49	26	6	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.434 (0.235, 0.802)
P-value: 0.00619

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Nervous system disorders (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

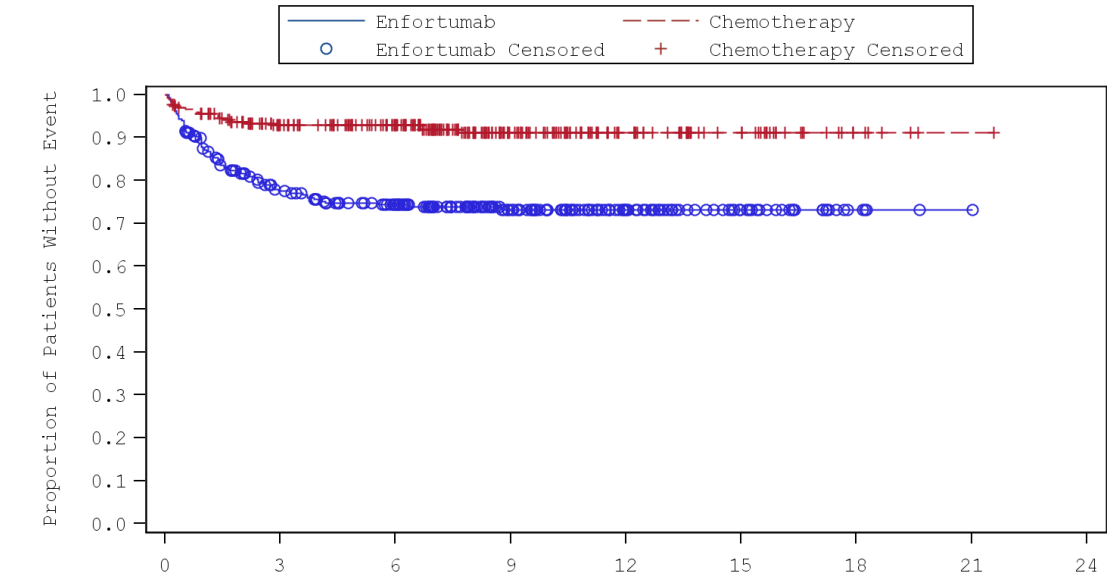
Enfortumab:	296	124	74	30	15	7	2	0	0
Chemotherapy:	291	139	97	43	17	9	3	1	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 1.424 (1.140, 1.778)
P-value: 0.00173

Enfortumab Median (95% CI): 2.83 (2.20, 3.68)
Chemotherapy Median (95% CI): 6.97 (3.94, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Nervous system disorders: Dysgeusia (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

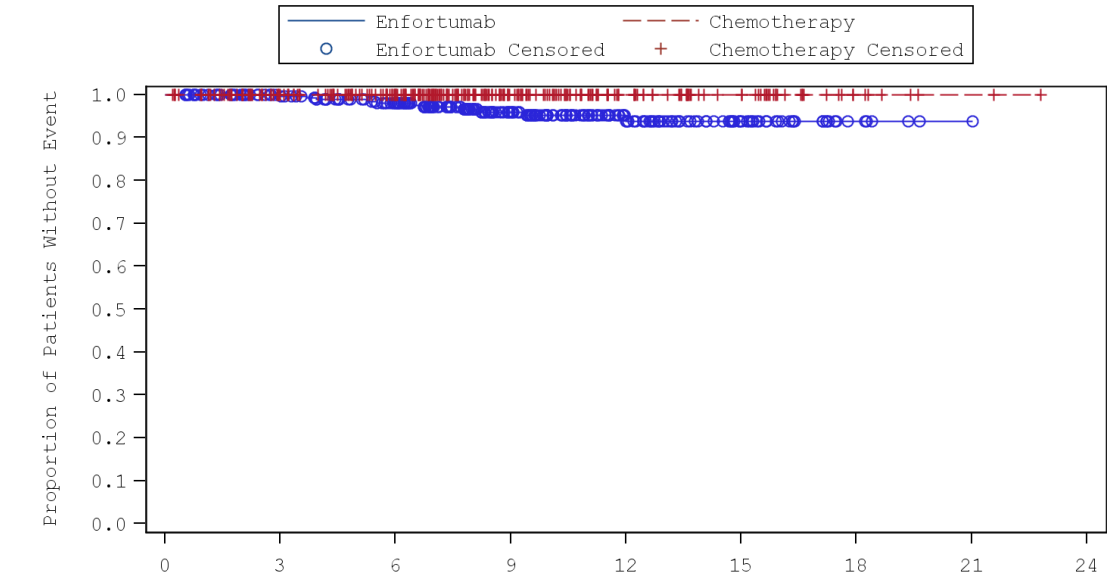
Enfortumab:	296	201	166	100	52	25	5	1	0
Chemotherapy:	291	229	189	99	52	27	6	1	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 3.412 (2.134, 5.457)
P-value: <.00001

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Nervous system disorders: Peripheral motor neuropathy (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

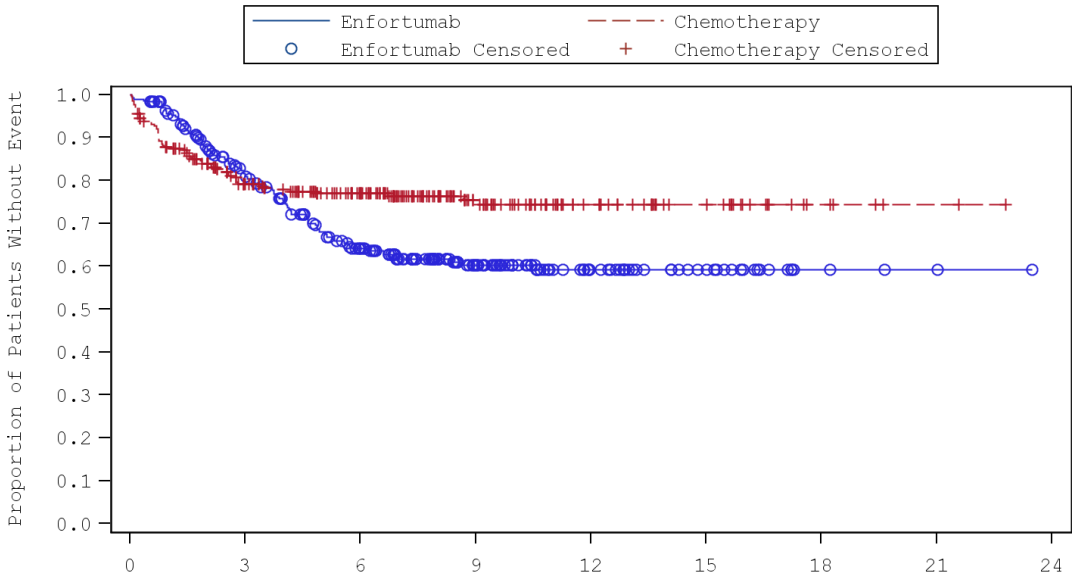
Enfortumab:	296	262	227	133	66	30	6	1	0
Chemotherapy:	291	248	204	109	57	31	7	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): NA (NA, NA)
P-value: 0.00302

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Nervous system disorders: Peripheral sensory neuropathy (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

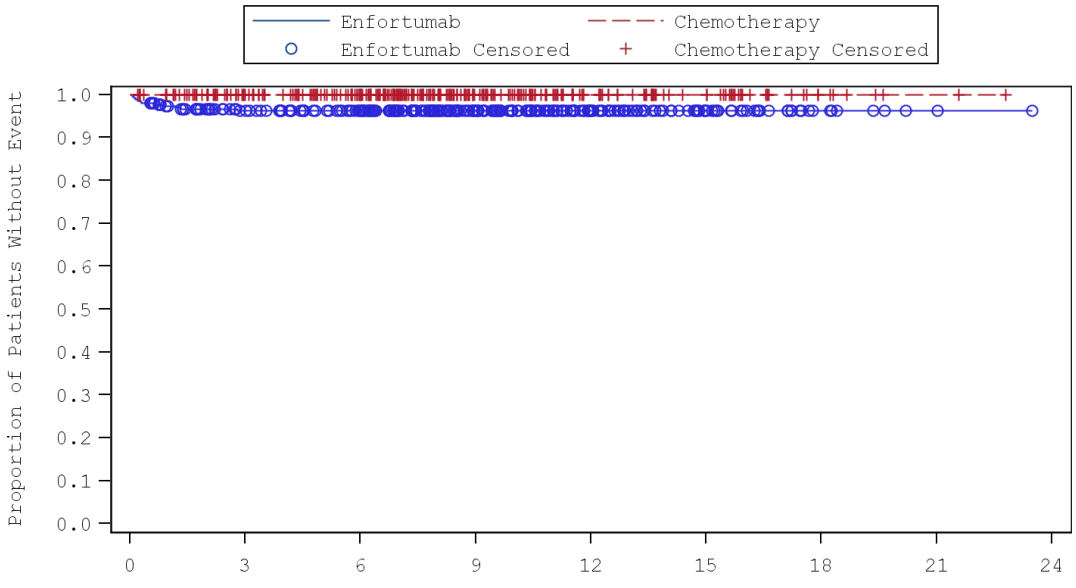
Enfortumab:	296	210	143	77	36	19	4	2	0
Chemotherapy:	291	192	146	74	37	21	6	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 1.425 (1.043, 1.945)
P-value: 0.02441

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Nervous system disorders: Taste disorder (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

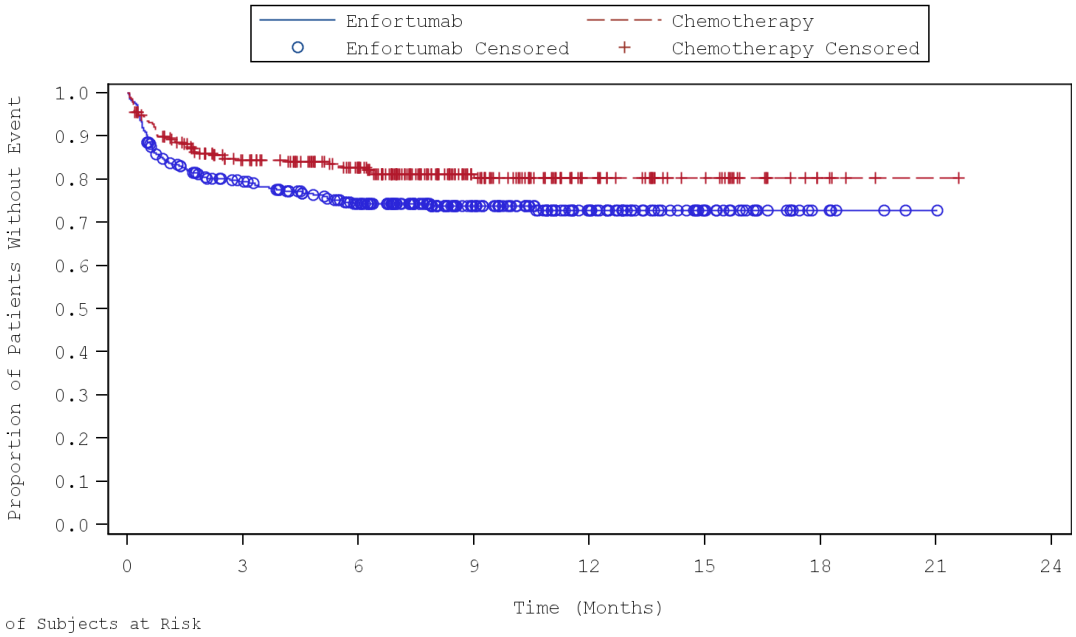
Enfortumab:	296	253	222	132	68	31	8	2	0
Chemotherapy:	291	248	204	109	57	31	7	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): NA (NA, NA)
P-value: 0.00084

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Renal and urinary disorders (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

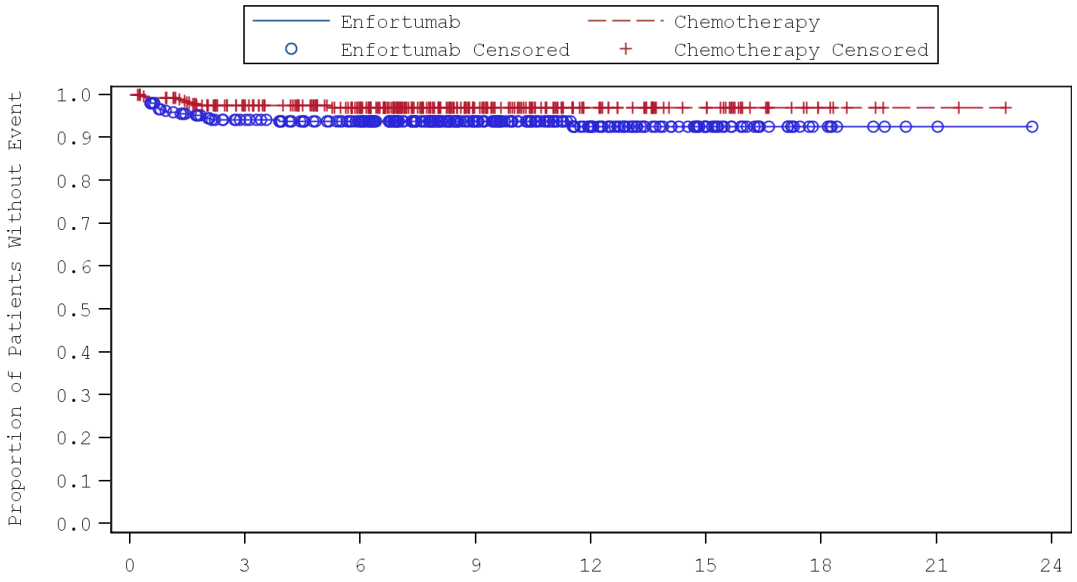
Enfortumab:	296	214	175	102	57	26	6	1	0
Chemotherapy:	291	213	175	91	44	24	5	1	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 1.437 (1.008, 2.049)
P-value: 0.04362

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Renal and urinary disorders: Acute kidney injury (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

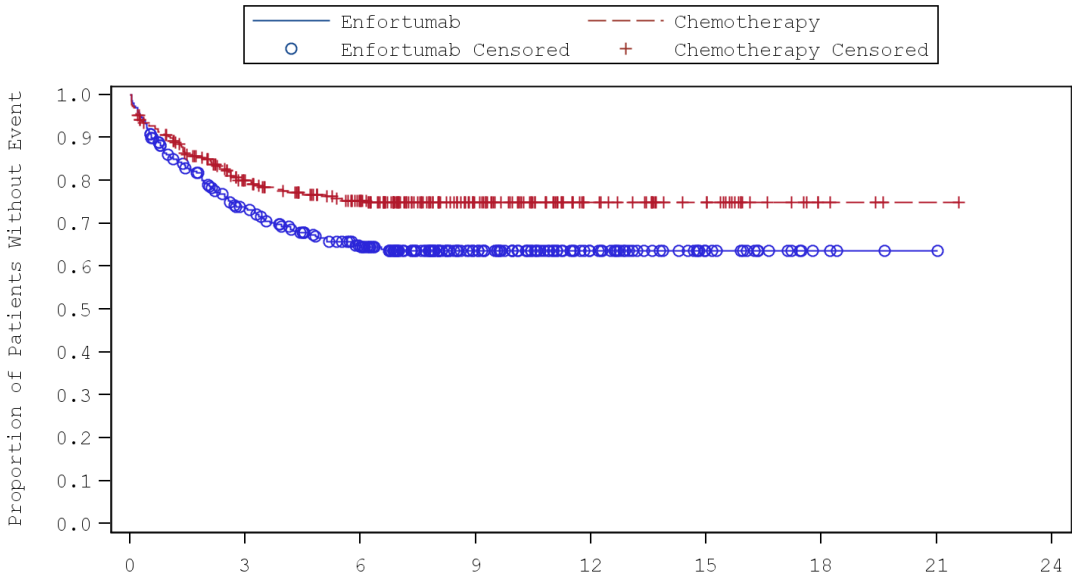
Enfortumab:	296	253	222	132	72	34	9	2	0
Chemotherapy:	291	245	202	108	56	31	7	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 2.337 (1.022, 5.344)
P-value: 0.03822

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Respiratory, thoracic and mediastinal disorders (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

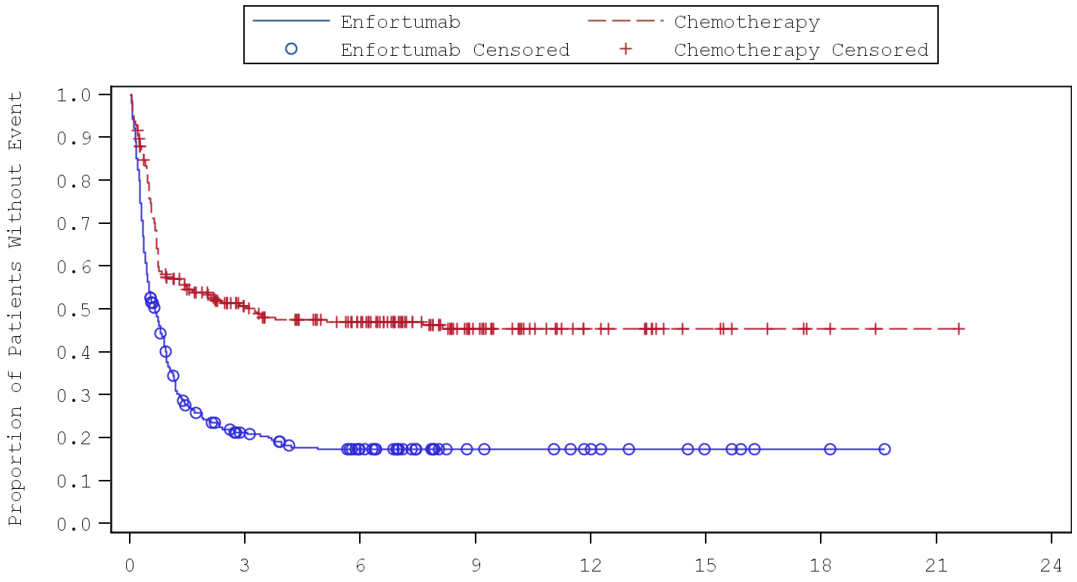
Enfortumab:	296	198	152	85	43	18	4	1	0
Chemotherapy:	291	200	158	83	39	23	4	1	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 1.482 (1.088, 2.018)
P-value: 0.01190

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Skin and subcutaneous tissue disorders (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

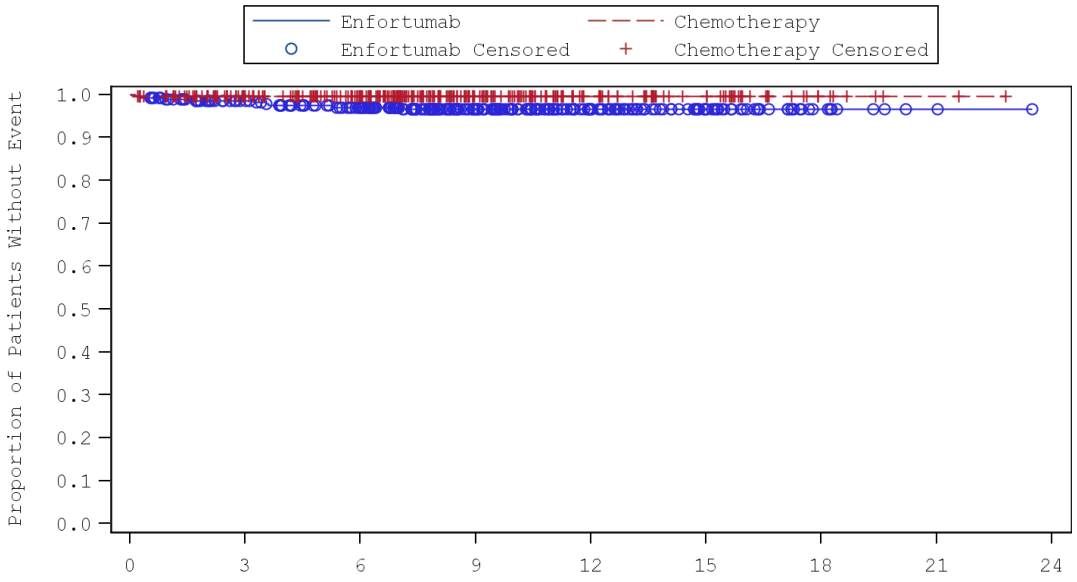
Enfortumab:	296	51	32	14	9	5	2	0	0
Chemotherapy:	291	116	88	40	19	9	3	1	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 2.217 (1.800, 2.732)
P-value: <.00001

Enfortumab Median (95% CI): 0.66 (0.49, 0.79)
Chemotherapy Median (95% CI): 3.12 (1.41, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Skin and subcutaneous tissue disorders: Blister (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

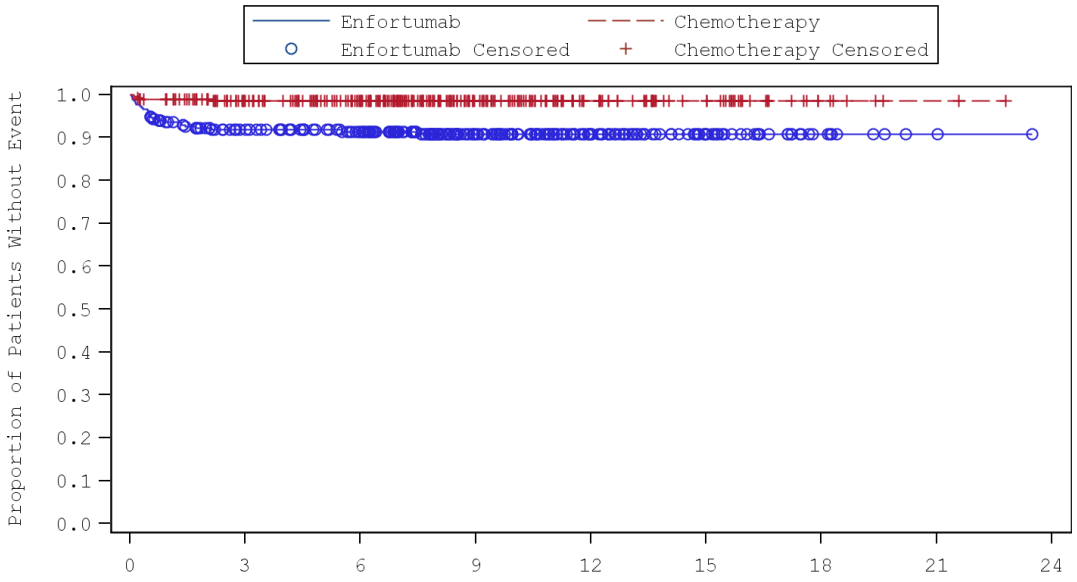
Enfortumab:	296	260	225	135	72	35	9	2	0
Chemotherapy:	291	247	203	109	57	31	7	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 8.901 (1.127, 70.273)
P-value: 0.01202

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Skin and subcutaneous tissue disorders: Drug eruption (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

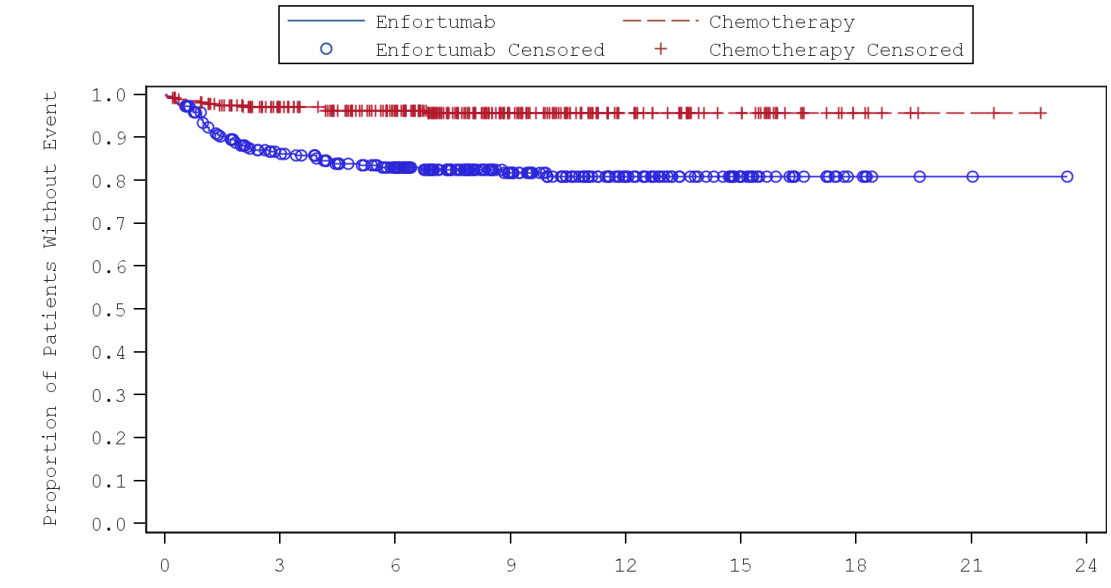
Enfortumab:	296	241	211	124	67	32	9	2	0
Chemotherapy:	291	244	200	107	57	31	7	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 6.765 (2.360, 19.394)
P-value: 0.00004

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Skin and subcutaneous tissue disorders: Dry skin (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

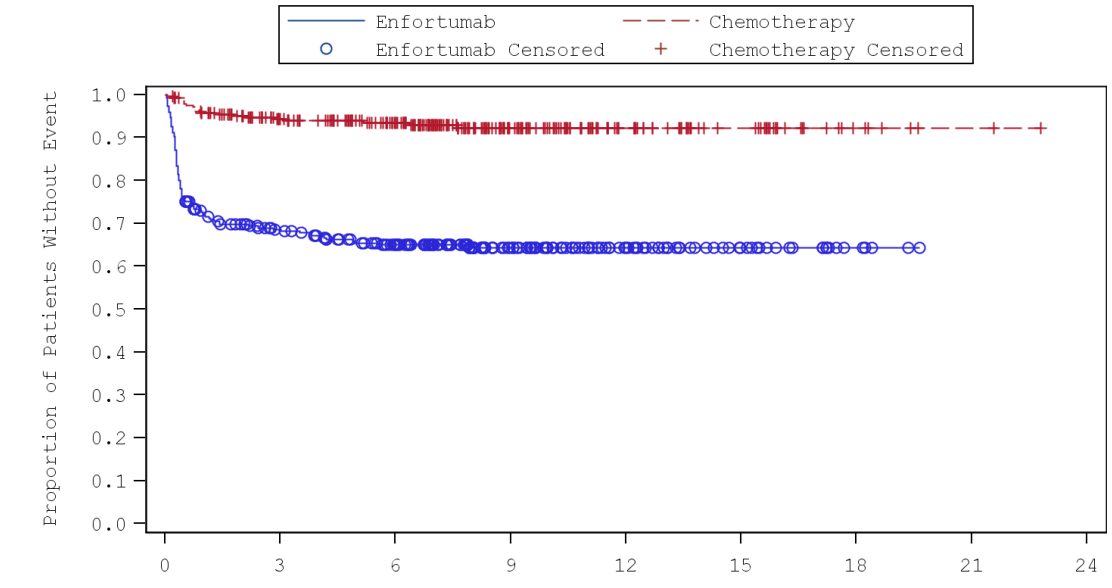
Enfortumab:	296	225	189	107	59	28	7	2	0
Chemotherapy:	291	241	197	106	54	30	7	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 4.639 (2.410, 8.928)
P-value: <.00001

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Skin and subcutaneous tissue disorders: Pruritus (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

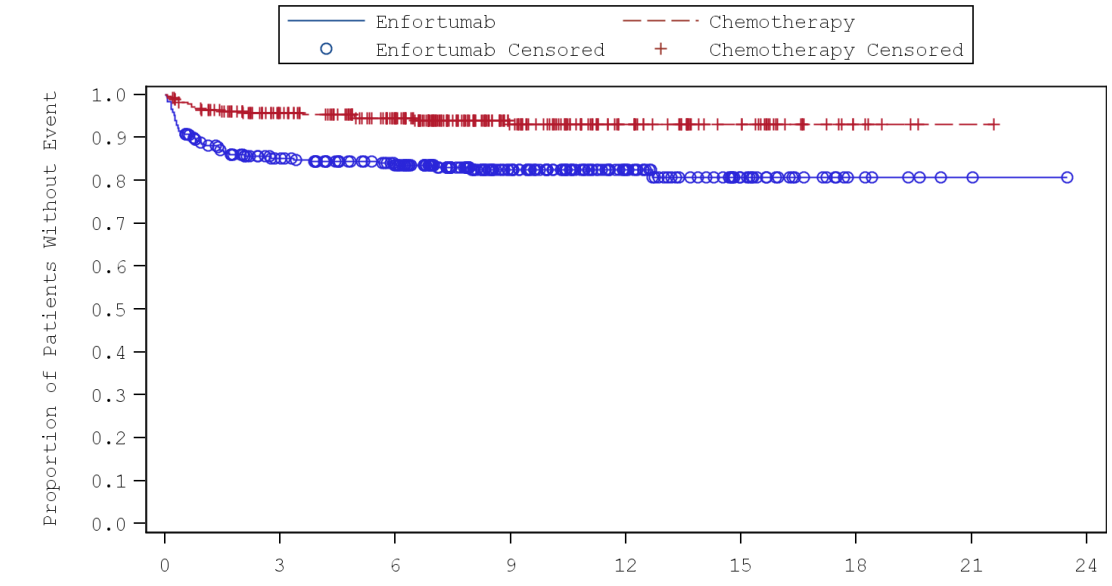
Enfortumab:	296	179	145	82	43	20	5	0	0
Chemotherapy:	291	233	189	99	50	27	7	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 6.363 (3.929, 10.304)
P-value: <.00001

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Skin and subcutaneous tissue disorders: Rash (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

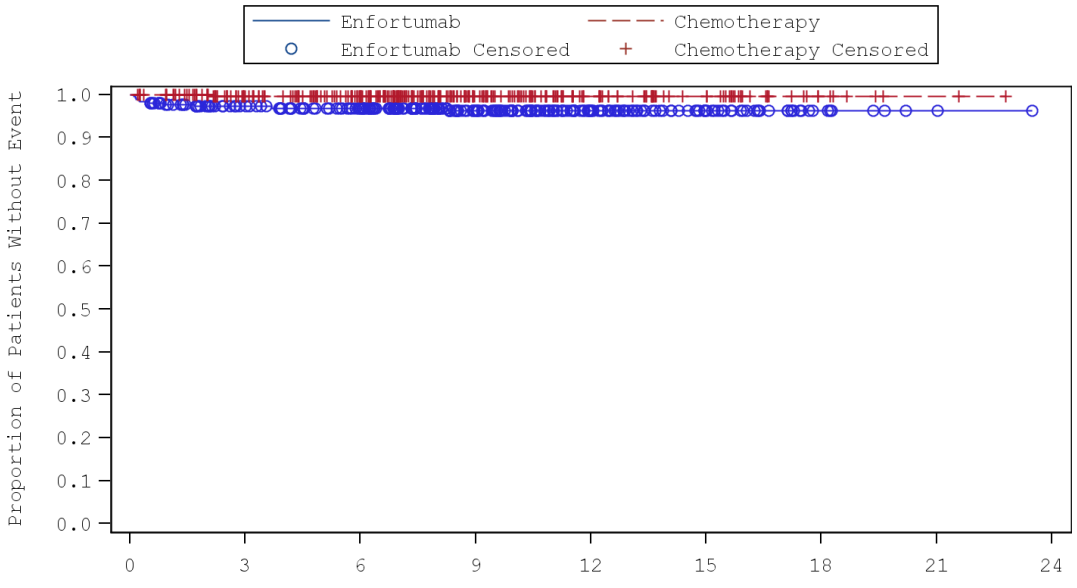
Enfortumab:	296	223	191	113	57	26	7	2	0
Chemotherapy:	291	236	192	100	53	29	6	1	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 3.063 (1.765, 5.315)
P-value: 0.00003

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Skin and subcutaneous tissue disorders: Rash erythematous (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

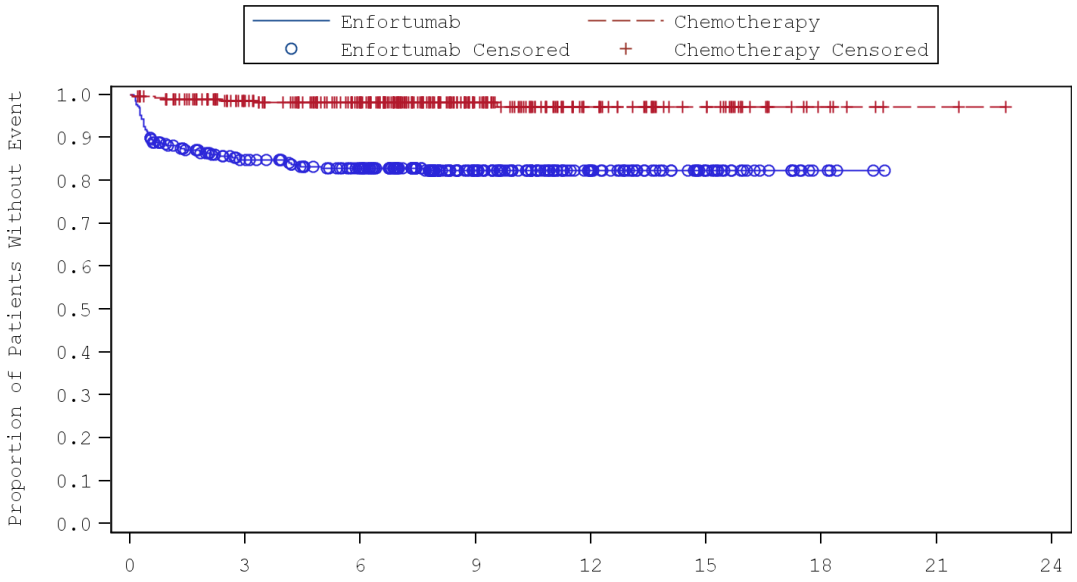
Enfortumab:	296	255	223	136	70	33	8	2	0
Chemotherapy:	291	247	203	109	57	31	7	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 9.790 (1.252, 76.579)
P-value: 0.00750

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Skin and subcutaneous tissue disorders: Rash maculo-papular (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

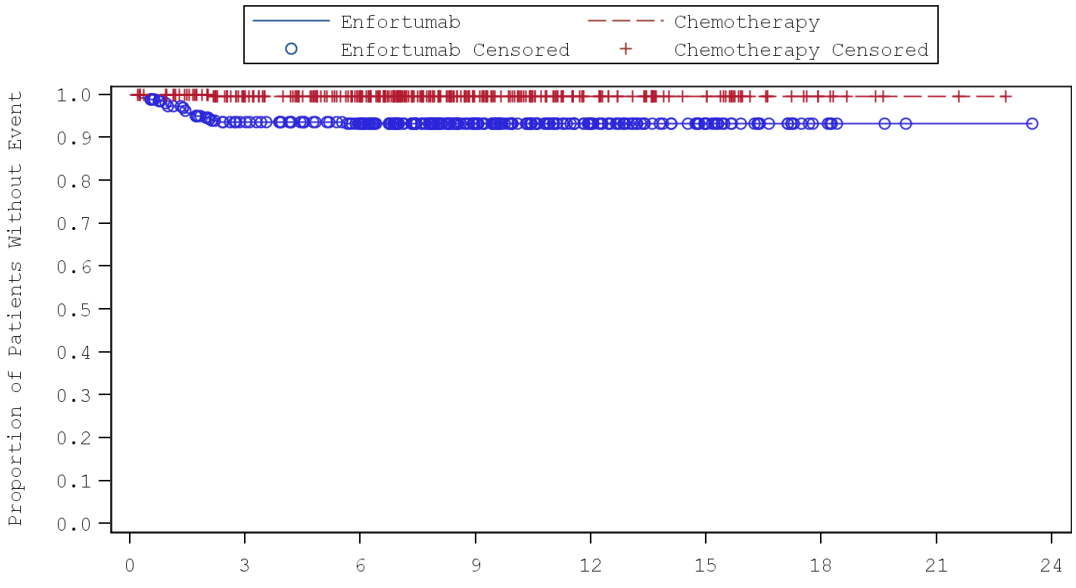
Enfortumab:	296	222	190	112	58	27	5	0	0
Chemotherapy:	291	244	199	105	54	30	7	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 9.396 (4.011, 22.011)
P-value: <.00001

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

Astellas: 7465-CL-0301
Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - Skin and subcutaneous tissue disorders: Skin hyperpigmentation (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

Enfortumab:	296	245	215	127	65	30	7	1	0
Chemotherapy:	291	247	203	108	56	30	7	2	0

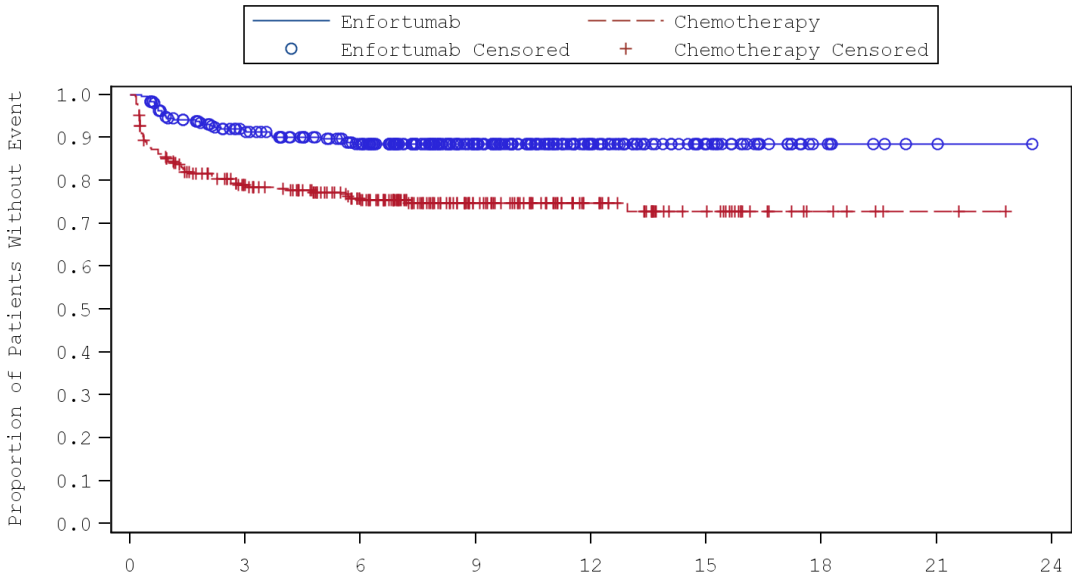
Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 20.704 (2.763, 155.151)
P-value: 0.00003

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_TEAE_KM_SAF

4.1.2 Schwer

Astellas: 7465-CL-0301
Figure AESV.KM.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) - Blood and lymphatic system disorders (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

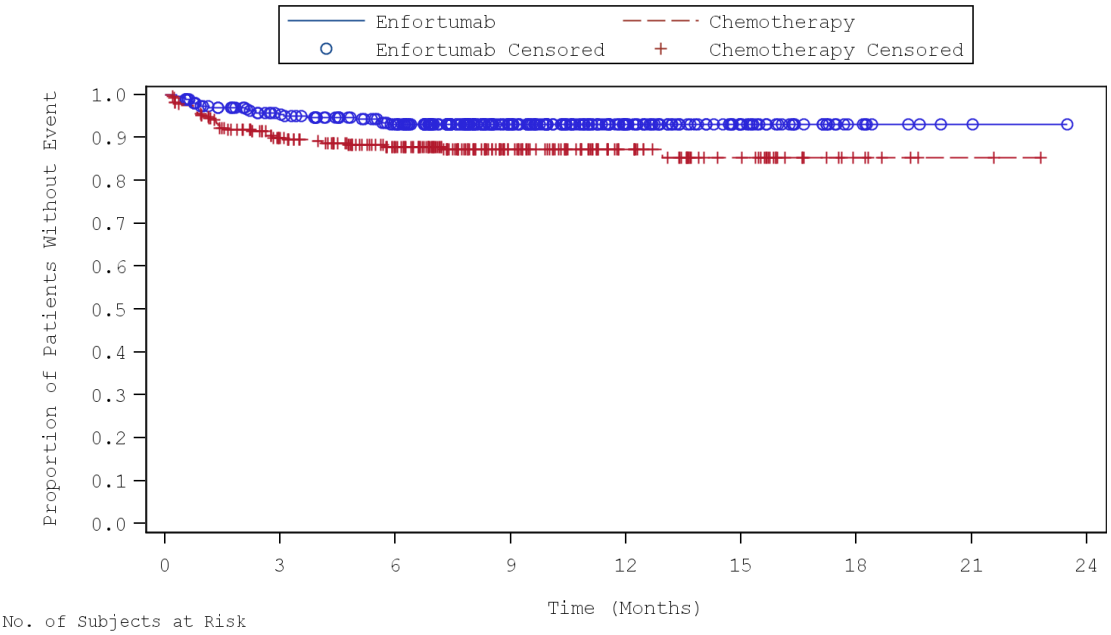
Enfortumab:	296	245	209	128	66	32	8	2	0
Chemotherapy:	291	200	158	85	45	23	6	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.388 (0.255, 0.591)
P-value: <.00001

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_AESV_KM_SAF

Astellas: 7465-CL-0301
Figure AESV.KM.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) - Blood and lymphatic system disorders: Anaemia (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

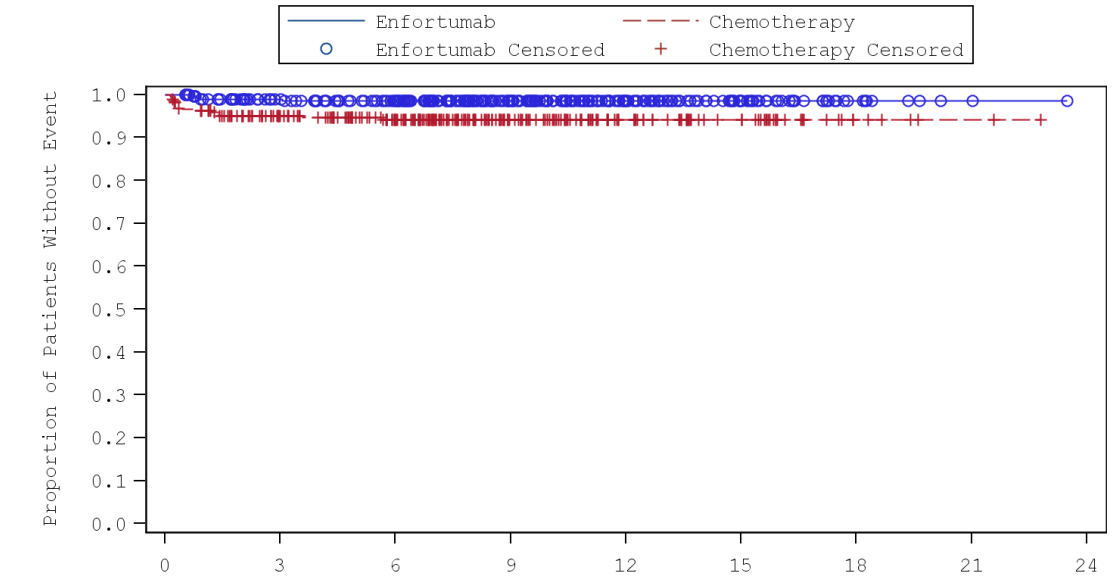
Enfortumab:	296	256	222	136	72	35	9	2	0
Chemotherapy:	291	226	181	99	52	28	7	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.487 (0.278, 0.856)
P-value: 0.01064

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_AESV_KM_SAF

Astellas: 7465-CL-0301
Figure AESV.KM.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) - Blood and lymphatic system disorders: Febrile neutropenia (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

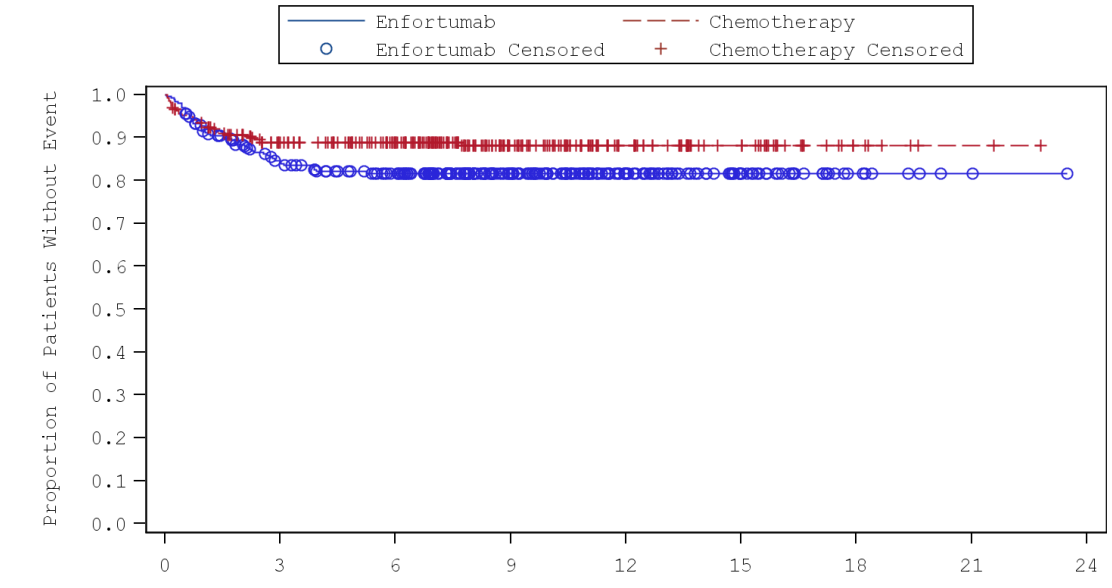
Enfortumab:	296	261	230	141	74	35	9	2	0
Chemotherapy:	291	236	193	103	56	30	6	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.234 (0.078, 0.700)
P-value: 0.00464

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_AESV_KM_SAF

Astellas: 7465-CL-0301
Figure AESV.KM.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) - Infections and infestations (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

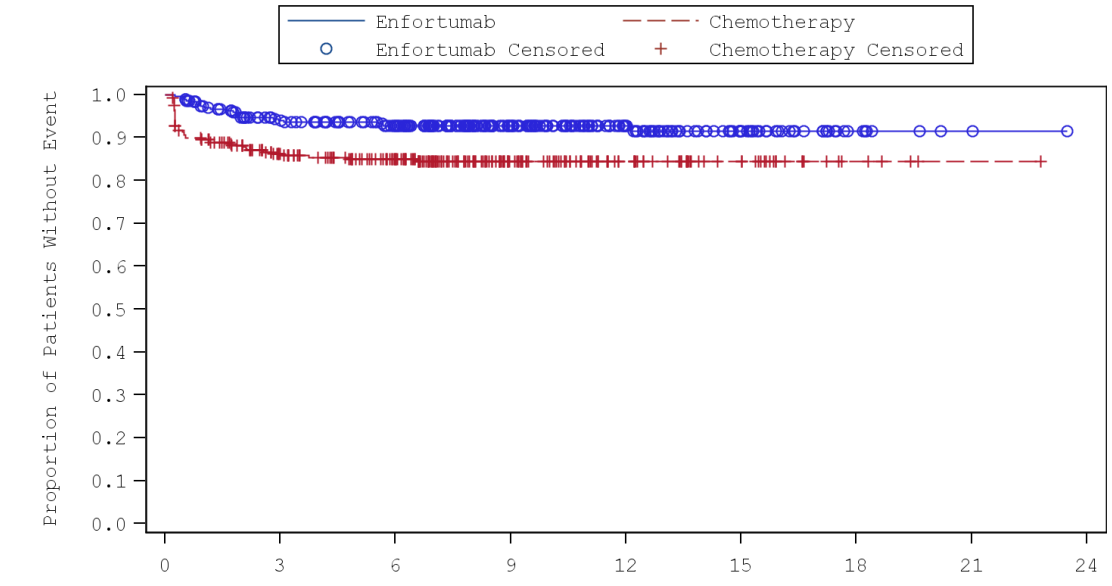
Enfortumab:	296	229	200	125	67	32	8	2	0
Chemotherapy:	291	229	189	104	56	30	7	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 1.568 (1.013, 2.428)
P-value: 0.04146

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_AESV_KM_SAF

Astellas: 7465-CL-0301
Figure AESV.KM.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) - Investigations: Neutrophil count decreased (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

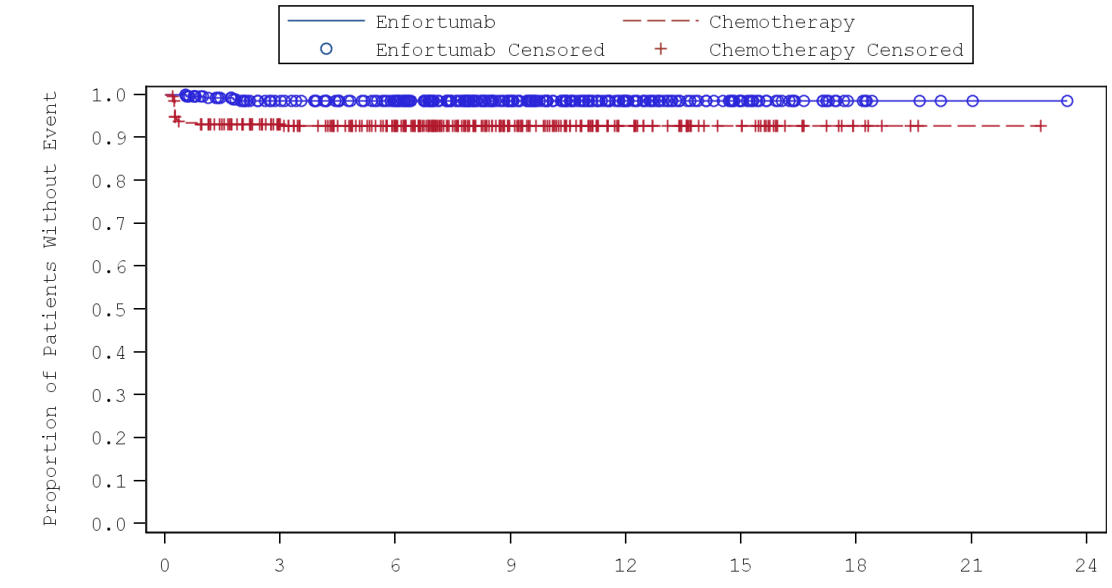
Enfortumab:	296	248	215	130	69	33	8	2	0
Chemotherapy:	291	211	169	87	46	23	5	1	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.414 (0.245, 0.700)
P-value: 0.00075

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_AESV_KM_SAF

Astellas: 7465-CL-0301
Figure AESV.KM.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) - Investigations: White blood cell count decreased (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

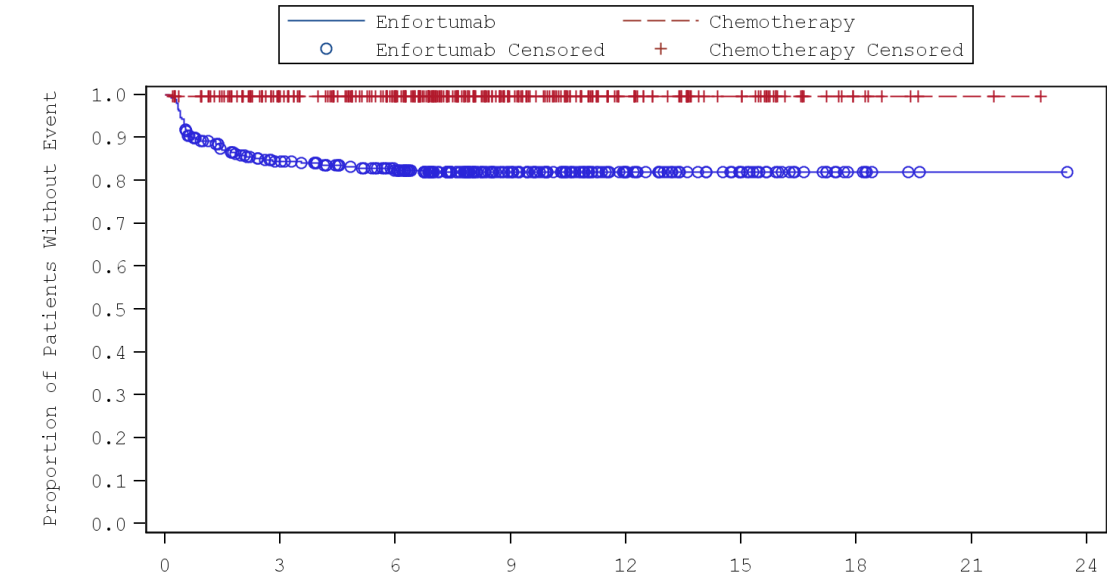
Enfortumab:	296	259	229	140	73	34	8	2	0
Chemotherapy:	291	229	189	101	52	28	6	1	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.181 (0.062, 0.527)
P-value: 0.00043

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_AESV_KM_SAF

Astellas: 7465-CL-0301
Figure AESV.KM.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) - Skin and subcutaneous tissue disorders (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

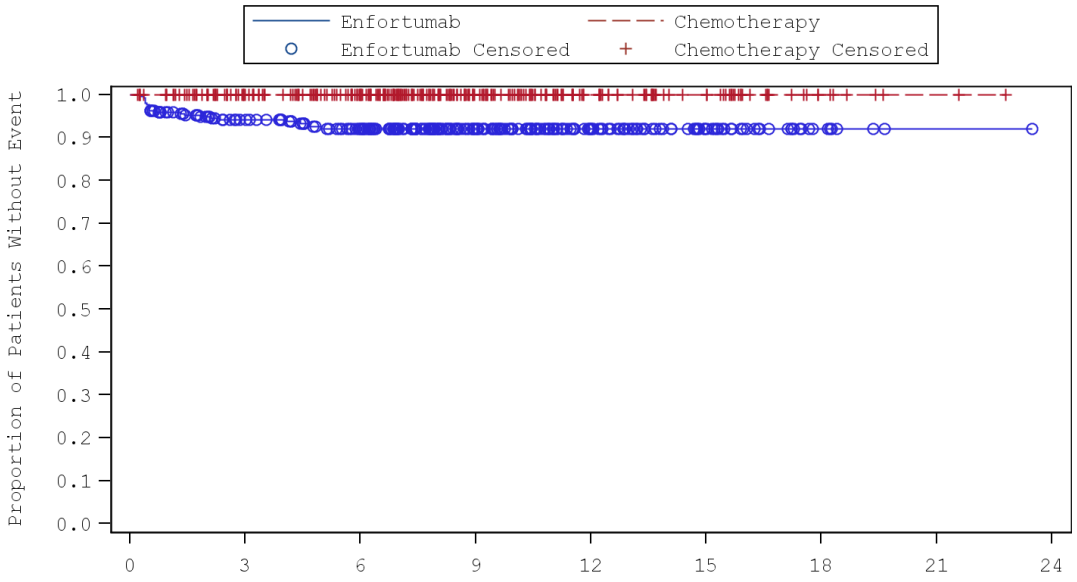
Enfortumab:	296	221	188	104	53	29	7	1	0
Chemotherapy:	291	247	203	108	57	31	7	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 56.180 (7.742, 407.667)
P-value: <.00001

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_AESV_KM_SAF

Astellas: 7465-CL-0301
Figure AESV.KM.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) - Skin and subcutaneous tissue disorders: Rash maculo-papular (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

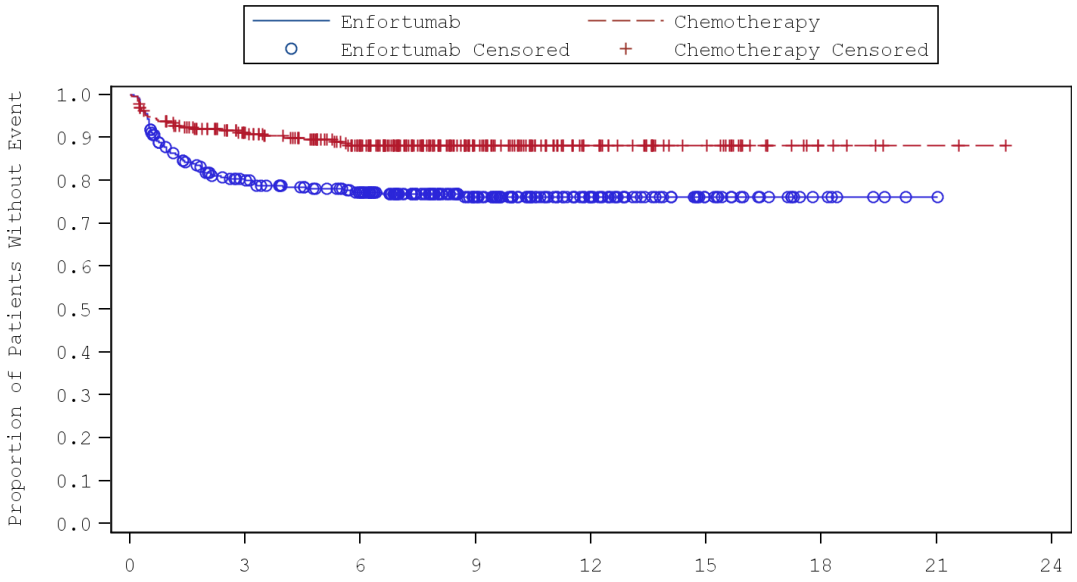
Enfortumab:	296	248	214	125	65	31	7	1	0
Chemotherapy:	291	248	204	109	57	31	7	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): NA (NA, NA)
P-value: <.00001

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_AESV_KM_SAF

Astellas: 7465-CL-0301
Figure AESV.KM.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) - Metabolism and nutrition disorders (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

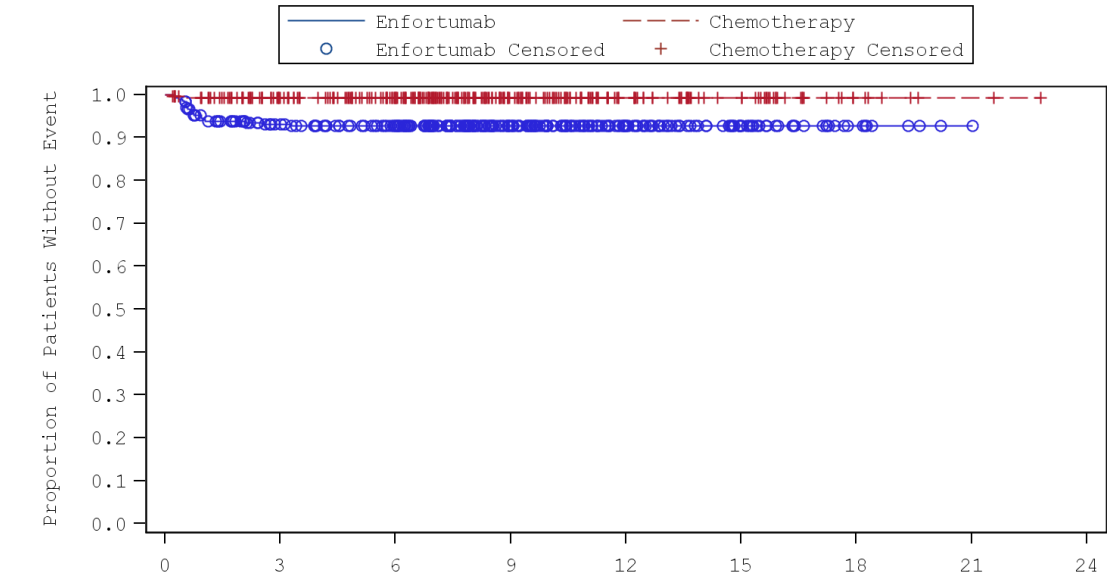
Enfortumab:	296	215	185	107	55	24	7	1	0
Chemotherapy:	291	228	181	96	49	27	6	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 2.087 (1.368, 3.183)
P-value: 0.00047

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_AESV_KM_SAF

Astellas: 7465-CL-0301
Figure AESV.KM.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) - Metabolism and nutrition disorders: Hyperglycaemia (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

Enfortumab:	296	246	217	128	66	30	8	1	0
Chemotherapy:	291	247	204	109	57	31	7	2	0

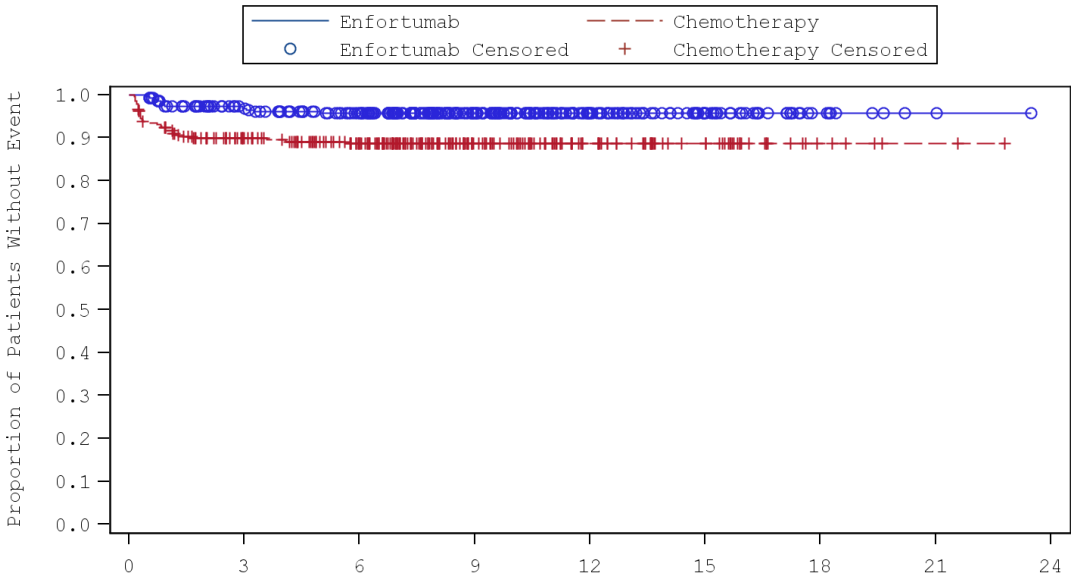
Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 10.395 (2.436, 44.354)
P-value: 0.00008

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_AESV_KM_SAF

4.1.3 Schwerwiegend

Astellas: 7465-CL-0301
Figure SAE.KM.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) - Blood and lymphatic system disorders (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

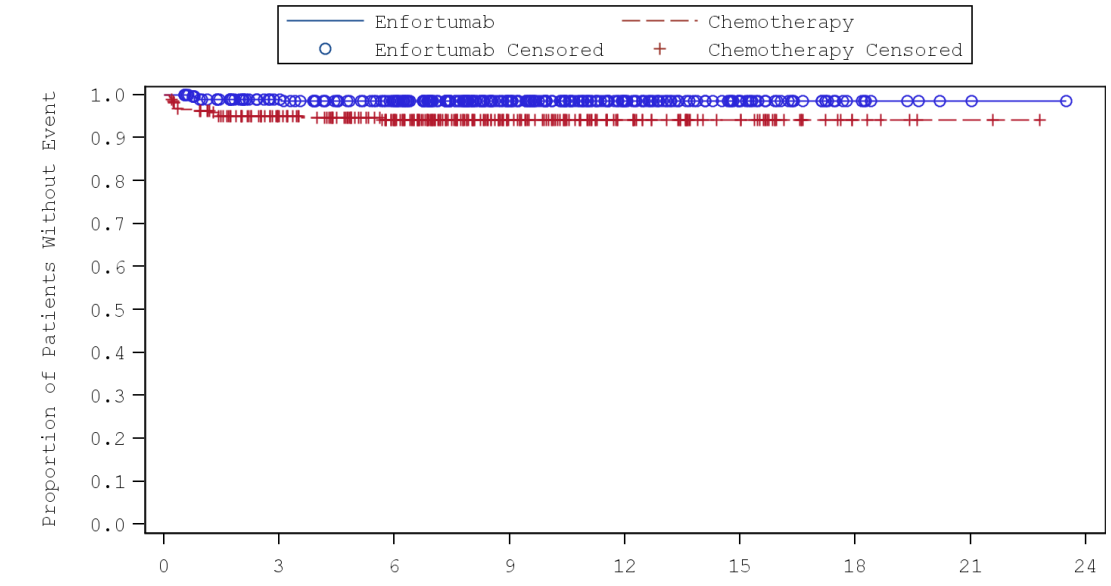
Enfortumab:	296	256	224	136	70	34	9	2	0
Chemotherapy:	291	226	186	100	55	29	6	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.335 (0.172, 0.654)
P-value: 0.00078

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_SAE_KM_SAF

Astellas: 7465-CL-0301
Figure SAE.KM.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) - Blood and lymphatic system disorders: Febrile neutropenia (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

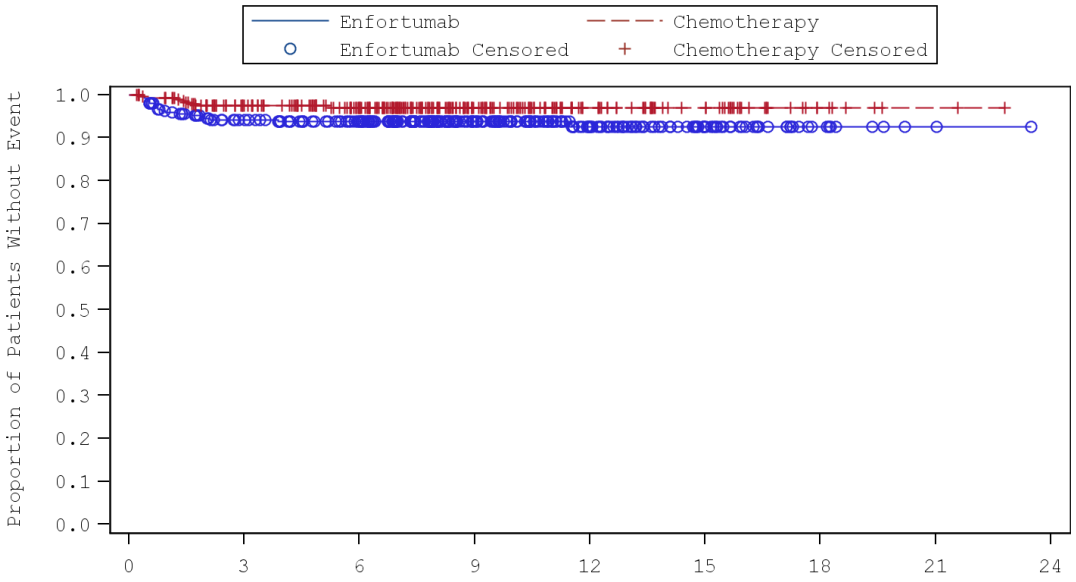
Enfortumab:	296	261	230	141	74	35	9	2	0
Chemotherapy:	291	236	193	103	56	30	6	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.234 (0.078, 0.700)
P-value: 0.00464

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_SAE_KM_SAF

Astellas: 7465-CL-0301
Figure SAE.KM.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) - Renal and urinary disorders: Acute kidney injury (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

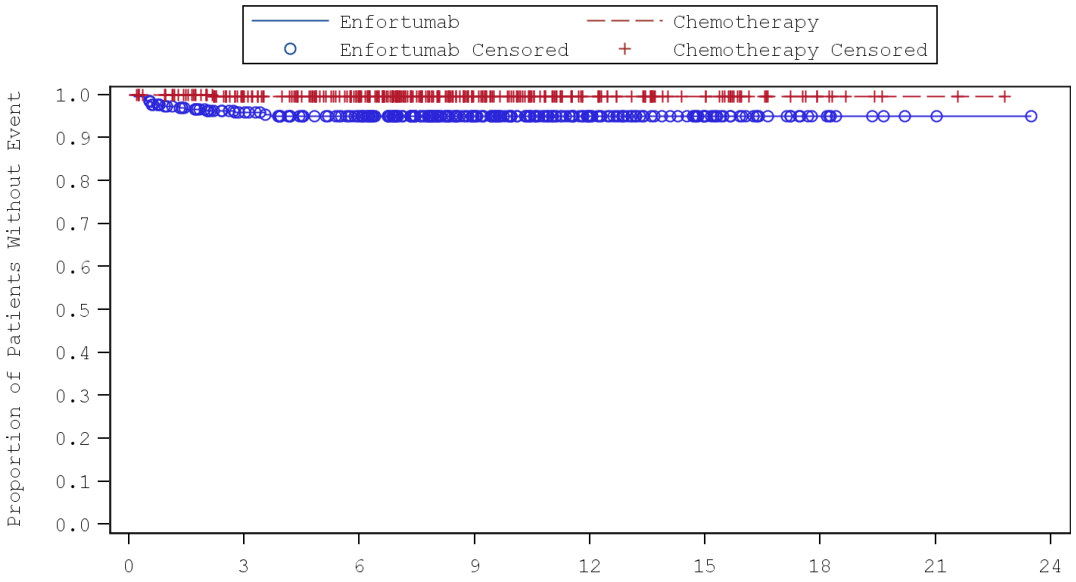
Enfortumab:	296	253	222	132	72	34	9	2	0
Chemotherapy:	291	245	202	108	56	31	7	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 2.337 (1.022, 5.344)
P-value: 0.03822

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_SAE_KM_SAF

Astellas: 7465-CL-0301
Figure SAE.KM.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) - Skin and subcutaneous tissue disorders (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

Enfortumab:	296	252	220	132	68	33	9	2	0
Chemotherapy:	291	247	204	109	57	31	7	2	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 14.228 (1.870, 108.274)
P-value: 0.00072

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (NC, NC)

NA: Not Available. NC: Not Calculable.
Reference Table: Tab_SAE_KM_SAF

4.2 Unerwünschte Ereignisse inkl. SOC und PT – Hauptebene und Subgruppenanalysen

Astellas: 7465-CL-0301
Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Any Event	No. of Events (%)	290 (98.0)	288 (99.0)
	Median Survival Est. (95% CI)	0.20 (0.16, 0.23)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.921 (0.779, 1.090)
	Treatment P-value [b]		0.41926
	Homogeneity P-value [c]		0.01636
Blood and lymphatic system disorders	No. of Events (%)	85 (28.7)	123 (42.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (7.06, NC)
	Hazard Ratio (95% CI) [a]		0.586 (0.443, 0.774)
	Treatment P-value [b]		0.00014
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Anaemia	No. of Events (%)	60 (20.3)	87 (29.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.626 (0.450, 0.872)
	Treatment P-value [b]		0.00529
	Homogeneity P-value [c]		NA
Febrile neutropenia	No. of Events (%)	4 (1.4)	16 (5.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.234 (0.078, 0.700)
	Treatment P-value [b]		0.00464
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Leukopenia	No. of Events (%)	2 (0.7)	8 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.241 (0.051, 1.135)
	Treatment P-value [b]		0.05070
	Homogeneity P-value [c]		NA
Neutropenia	No. of Events (%)	20 (6.8)	28 (9.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.666 (0.375, 1.184)
	Treatment P-value [b]		0.16353
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Thrombocytopenia	No. of Events (%)	10 (3.4)	7 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.359 (0.515, 3.583)
	Treatment P-value [b]		0.53366
	Homogeneity P-value [c]		NA
Cardiac disorders	No. of Events (%)	23 (7.8)	16 (5.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.425 (0.752, 2.700)
	Treatment P-value [b]		0.27484
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Ear and labyrinth disorders	No. of Events (%)	9 (3.0)	4 (1.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.990 (0.606, 6.531)
	Treatment P-value [b]		0.24733
	Homogeneity P-value [c]		NA
Endocrine disorders	No. of Events (%)	7 (2.4)	6 (2.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.941 (0.306, 2.895)
	Treatment P-value [b]		0.91610
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Eye disorders	No. of Events (%)	80 (27.0)	26 (8.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.436 (2.204, 5.356)
	Treatment P-value [b]		<.00001
	Homogeneity P-value [c]		NA
Dry eye	No. of Events (%)	19 (6.4)	3 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.120 (1.810, 20.696)
	Treatment P-value [b]		0.00088
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Lacrimation increased	No. of Events (%)	30 (10.1)	12 (4.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.400 (1.226, 4.700)
	Treatment P-value [b]		0.00842
	Homogeneity P-value [c]		NA
Vision blurred	No. of Events (%)	16 (5.4)	5 (1.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.199 (1.170, 8.750)
	Treatment P-value [b]		0.01668
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Gastrointestinal disorders	No. of Events (%)	207 (69.9)	183 (62.9)
	Median Survival Est. (95% CI)	0.85 (0.66, 1.22)	1.35 (0.72, 2.00)
	Hazard Ratio (95% CI) [a]		1.067 (0.873, 1.305)
	Treatment P-value [b]		0.49812
	Homogeneity P-value [c]		NA
Abdominal pain	No. of Events (%)	40 (13.5)	27 (9.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.427 (0.875, 2.328)
	Treatment P-value [b]		0.15330
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
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Astellas: 7465-CL-0301
Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Abdominal pain upper	No. of Events (%)	12 (4.1)	8 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.474 (0.602, 3.609)
	Treatment P-value [b]		0.39018
	Homogeneity P-value [c]		NA
Constipation	No. of Events (%)	83 (28.0)	74 (25.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.070 (0.781, 1.467)
	Treatment P-value [b]		0.65321
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Diarrhoea	No. of Events (%)	103 (34.8)	67 (23.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.598 (1.174, 2.177)
	Treatment P-value [b]		0.00277
	Homogeneity P-value [c]		NA
Dry mouth	No. of Events (%)	24 (8.1)	7 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.251 (1.397, 7.565)
	Treatment P-value [b]		0.00393
	Homogeneity P-value [c]		NA

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The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Dyspepsia	No. of Events (%)	19 (6.4)	9 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.076 (0.938, 4.594)
	Treatment P-value [b]		0.06517
	Homogeneity P-value [c]		NA
Gastrooesophageal reflux disease	No. of Events (%)	6 (2.0)	4 (1.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.356 (0.381, 4.824)
	Treatment P-value [b]		0.63644
	Homogeneity P-value [c]		NA

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Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Nausea	No. of Events (%)	90 (30.4)	75 (25.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.157 (0.851, 1.573)
	Treatment P-value [b]		0.35226
	Homogeneity P-value [c]		NA
Stomatitis	No. of Events (%)	27 (9.1)	21 (7.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.257 (0.710, 2.224)
	Treatment P-value [b]		0.43091
	Homogeneity P-value [c]		NA

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Analysis Plan: 15FEB2021 Confidential

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Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Vomiting	No. of Events (%)	43 (14.5)	44 (15.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.945 (0.620, 1.440)
	Treatment P-value [b]		0.78782
	Homogeneity P-value [c]		NA
General disorders and administration site conditions	No. of Events (%)	210 (70.9)	187 (64.3)
	Median Survival Est. (95% CI)	1.28 (0.89, 1.74)	1.18 (0.79, 2.07)
	Hazard Ratio (95% CI) [a]		1.056 (0.866, 1.288)
	Treatment P-value [b]		0.57157
	Homogeneity P-value [c]		NA

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Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Asthenia	No. of Events (%)	46 (15.5)	40 (13.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.008 (0.658, 1.545)
	Treatment P-value [b]		0.96084
	Homogeneity P-value [c]		NA
Chills	No. of Events (%)	17 (5.7)	6 (2.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.657 (1.046, 6.748)
	Treatment P-value [b]		0.03256
	Homogeneity P-value [c]		NA

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Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Fatigue	No. of Events (%)	108 (36.5)	78 (26.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.376 (1.027, 1.843)
	Treatment P-value [b]		0.03176
	Homogeneity P-value [c]		NA
General physical health deterioration	No. of Events (%)	7 (2.4)	11 (3.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.593 (0.230, 1.533)
	Treatment P-value [b]		0.27584
	Homogeneity P-value [c]		NA

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Analysis Plan: 15FEB2021 Confidential

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Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Influenza like illness	No. of Events (%)	7 (2.4)	3 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.178 (0.562, 8.433)
	Treatment P-value [b]		0.24789
	Homogeneity P-value [c]		NA
Malaise	No. of Events (%)	13 (4.4)	21 (7.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.574 (0.287, 1.148)
	Treatment P-value [b]		0.11274
	Homogeneity P-value [c]		NA

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Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Mucosal inflammation	No. of Events (%)	14 (4.7)	14 (4.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.964 (0.459, 2.023)
	Treatment P-value [b]		0.92319
	Homogeneity P-value [c]		NA
Oedema peripheral	No. of Events (%)	27 (9.1)	39 (13.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.639 (0.390, 1.046)
	Treatment P-value [b]		0.07321
	Homogeneity P-value [c]		NA

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Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Pain	No. of Events (%)	4 (1.4)	9 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.435 (0.134, 1.415)
	Treatment P-value [b]		0.15461
	Homogeneity P-value [c]		NA
Pyrexia	No. of Events (%)	65 (22.0)	43 (14.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.440 (0.978, 2.121)
	Treatment P-value [b]		0.06319
	Homogeneity P-value [c]		NA

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Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Hepatobiliary disorders	No. of Events (%)	14 (4.7)	9 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.493 (0.645, 3.452)
	Treatment P-value [b]		0.34591
	Homogeneity P-value [c]		NA
Infections and infestations	No. of Events (%)	152 (51.4)	105 (36.1)
	Median Survival Est. (95% CI)	6.08 (3.52, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.473 (1.147, 1.892)
	Treatment P-value [b]		0.00231
	Homogeneity P-value [c]		NA

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Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Cellulitis	No. of Events (%)	8 (2.7)	4 (1.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.931 (0.579, 6.432)
	Treatment P-value [b]		0.27545
	Homogeneity P-value [c]		NA
Conjunctivitis	No. of Events (%)	19 (6.4)	2 (0.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.898 (2.300, 42.589)
	Treatment P-value [b]		0.00015
	Homogeneity P-value [c]		NA

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Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Escherichia urinary tract infection	No. of Events (%)	7 (2.4)	4 (1.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.699 (0.497, 5.807)
	Treatment P-value [b]		0.39280
	Homogeneity P-value [c]		NA
Nasopharyngitis	No. of Events (%)	15 (5.1)	9 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.596 (0.697, 3.655)
	Treatment P-value [b]		0.26493
	Homogeneity P-value [c]		NA

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Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Oral candidiasis	No. of Events (%)	10 (3.4)	3 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.995 (0.821, 10.926)
	Treatment P-value [b]		0.08144
	Homogeneity P-value [c]		NA
Pneumonia	No. of Events (%)	20 (6.8)	11 (3.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.806 (0.864, 3.774)
	Treatment P-value [b]		0.11077
	Homogeneity P-value [c]		NA

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Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Upper respiratory tract infection	No. of Events (%)	7 (2.4)	9 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.698 (0.258, 1.886)
	Treatment P-value [b]		0.47795
	Homogeneity P-value [c]		NA
Urinary tract infection	No. of Events (%)	26 (8.8)	20 (6.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.284 (0.716, 2.303)
	Treatment P-value [b]		0.39972
	Homogeneity P-value [c]		NA

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Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Urinary tract infection bacterial	No. of Events (%)	20 (6.8)	12 (4.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.579 (0.771, 3.233)
	Treatment P-value [b]		0.20656
	Homogeneity P-value [c]		NA
Injury, poisoning and procedural complications	No. of Events (%)	38 (12.8)	33 (11.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.105 (0.692, 1.764)
	Treatment P-value [b]		0.67174
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Date/time of run: 20APR2021 13:50
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Astellas: 7465-CL-0301
Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Fall	No. of Events (%)	17 (5.7)	9 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.761 (0.783, 3.962)
	Treatment P-value [b]		0.16543
	Homogeneity P-value [c]		NA
Infusion related reaction	No. of Events (%)	6 (2.0)	11 (3.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.541 (0.200, 1.465)
	Treatment P-value [b]		0.22141
	Homogeneity P-value [c]		NA

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Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Investigations	No. of Events (%)	136 (45.9)	119 (40.9)
	Median Survival Est. (95% CI)	NC (4.86, NC)	NC (10.38, NC)
	Hazard Ratio (95% CI) [a]		1.029 (0.803, 1.318)
	Treatment P-value [b]		0.79525
	Homogeneity P-value [c]		NA
Alanine aminotransferase increased	No. of Events (%)	27 (9.1)	5 (1.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.272 (2.026, 13.715)
	Treatment P-value [b]		0.00014
	Homogeneity P-value [c]		NA

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Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Amylase increased	No. of Events (%)	11 (3.7)	2 (0.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.466 (1.208, 24.731)
	Treatment P-value [b]		0.01332
	Homogeneity P-value [c]		NA
Aspartate aminotransferase increased	No. of Events (%)	36 (12.2)	5 (1.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.237 (2.835, 18.474)
	Treatment P-value [b]		<.00001
	Homogeneity P-value [c]		NA

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Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Blood alkaline phosphatase increased	No. of Events (%)	8 (2.7)	10 (3.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.713 (0.279, 1.823)
	Treatment P-value [b]		0.47778
	Homogeneity P-value [c]		NA
Blood creatinine increased	No. of Events (%)	26 (8.8)	7 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.902 (1.690, 9.012)
	Treatment P-value [b]		0.00059
	Homogeneity P-value [c]		NA

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Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Lipase increased	No. of Events (%)	12 (4.1)	11 (3.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.067 (0.468, 2.430)
	Treatment P-value [b]		0.87804
	Homogeneity P-value [c]		NA
Lymphocyte count decreased	No. of Events (%)	14 (4.7)	17 (5.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.817 (0.402, 1.660)
	Treatment P-value [b]		0.57547
	Homogeneity P-value [c]		NA

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Analysis Plan: 15FEB2021 Confidential

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Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Neutrophil count decreased	No. of Events (%)	33 (11.1)	54 (18.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.507 (0.327, 0.785)
	Treatment P-value [b]		0.00215
	Homogeneity P-value [c]		NA
Platelet count decreased	No. of Events (%)	6 (2.0)	7 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.835 (0.280, 2.489)
	Treatment P-value [b]		0.74607
	Homogeneity P-value [c]		NA

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Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Weight decreased	No. of Events (%)	48 (16.2)	20 (6.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.357 (1.395, 3.981)
	Treatment P-value [b]		0.00097
	Homogeneity P-value [c]		NA
White blood cell count decreased	No. of Events (%)	16 (5.4)	32 (11.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.449 (0.246, 0.818)
	Treatment P-value [b]		0.00791
	Homogeneity P-value [c]		NA

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Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Metabolism and nutrition disorders	No. of Events (%)	174 (58.8)	126 (43.3)
	Median Survival Est. (95% CI)	2.17 (1.41, 4.11)	NC (6.05, NC)
	Hazard Ratio (95% CI) [a]		1.446 (1.149, 1.821)
	Treatment P-value [b]		0.00158
	Homogeneity P-value [c]		NA
Decreased appetite	No. of Events (%)	121 (40.9)	78 (26.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.542 (1.159, 2.052)
	Treatment P-value [b]		0.00262
	Homogeneity P-value [c]		NA

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Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Dehydration	No. of Events (%)	10 (3.4)	7 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.386 (0.527, 3.646)
	Treatment P-value [b]		0.50653
	Homogeneity P-value [c]		NA
Hypercalcaemia	No. of Events (%)	6 (2.0)	6 (2.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.934 (0.301, 2.898)
	Treatment P-value [b]		0.90572
	Homogeneity P-value [c]		NA

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Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Hyperglycaemia	No. of Events (%)	31 (10.5)	6 (2.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.134 (2.141, 12.312)
	Treatment P-value [b]		0.00004
	Homogeneity P-value [c]		NA
Hyperkalaemia	No. of Events (%)	9 (3.0)	12 (4.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.711 (0.299, 1.690)
	Treatment P-value [b]		0.43782
	Homogeneity P-value [c]		NA

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Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Hypoalbuminaemia	No. of Events (%)	14 (4.7)	10 (3.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.372 (0.609, 3.091)
	Treatment P-value [b]		0.44128
	Homogeneity P-value [c]		NA
Hypocalcaemia	No. of Events (%)	10 (3.4)	9 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.989 (0.401, 2.441)
	Treatment P-value [b]		0.98105
	Homogeneity P-value [c]		NA

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Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Hypokalaemia	No. of Events (%)	19 (6.4)	10 (3.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.883 (0.875, 4.052)
	Treatment P-value [b]		0.09967
	Homogeneity P-value [c]		NA
Hypomagnesaemia	No. of Events (%)	18 (6.1)	8 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.227 (0.967, 5.131)
	Treatment P-value [b]		0.05419
	Homogeneity P-value [c]		NA

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Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Hyponatraemia	No. of Events (%)	19 (6.4)	13 (4.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.323 (0.651, 2.687)
	Treatment P-value [b]		0.43754
	Homogeneity P-value [c]		NA
Hypophosphataemia	No. of Events (%)	12 (4.1)	10 (3.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.187 (0.512, 2.753)
	Treatment P-value [b]		0.68849
	Homogeneity P-value [c]		NA

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Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Musculoskeletal and connective tissue disorders	No. of Events (%)	100 (33.8)	120 (41.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (8.02, NC)
	Hazard Ratio (95% CI) [a]		0.682 (0.522, 0.892)
	Treatment P-value [b]		0.00531
	Homogeneity P-value [c]		NA
Arthralgia	No. of Events (%)	20 (6.8)	36 (12.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.479 (0.276, 0.834)
	Treatment P-value [b]		0.00785
	Homogeneity P-value [c]		NA

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The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Date/time of run: 20APR2021 13:50
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Astellas: 7465-CL-0301
Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Back pain	No. of Events (%)	28 (9.5)	26 (8.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.012 (0.590, 1.736)
	Treatment P-value [b]		0.96420
	Homogeneity P-value [c]		NA
Bone pain	No. of Events (%)	6 (2.0)	8 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.676 (0.234, 1.953)
	Treatment P-value [b]		0.47217
	Homogeneity P-value [c]		NA

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Analysis Plan: 15FEB2021 Confidential

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Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Flank pain	No. of Events (%)	7 (2.4)	6 (2.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.074 (0.361, 3.198)
	Treatment P-value [b]		0.90549
	Homogeneity P-value [c]		NA
Muscle spasms	No. of Events (%)	10 (3.4)	8 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.172 (0.462, 2.976)
	Treatment P-value [b]		0.73794
	Homogeneity P-value [c]		NA

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

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Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Muscular weakness	No. of Events (%)	16 (5.4)	7 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.085 (0.851, 5.108)
	Treatment P-value [b]		0.10018
	Homogeneity P-value [c]		NA
Musculoskeletal pain	No. of Events (%)	7 (2.4)	9 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.725 (0.270, 1.952)
	Treatment P-value [b]		0.52339
	Homogeneity P-value [c]		NA

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Analysis Plan: 15FEB2021 Confidential

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Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Myalgia	No. of Events (%)	15 (5.1)	32 (11.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.434 (0.235, 0.802)
	Treatment P-value [b]		0.00619
	Homogeneity P-value [c]		NA
Pain in extremity	No. of Events (%)	17 (5.7)	15 (5.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.064 (0.530, 2.134)
	Treatment P-value [b]		0.86286
	Homogeneity P-value [c]		NA

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Analysis Plan: 15FEB2021 Confidential

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Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	No. of Events (%)	23 (7.8)	24 (8.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.920 (0.518, 1.635)
	Treatment P-value [b]		0.77670
	Homogeneity P-value [c]		NA
Malignant neoplasm progression	No. of Events (%)	12 (4.1)	11 (3.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.062 (0.466, 2.418)
	Treatment P-value [b]		0.88597
	Homogeneity P-value [c]		NA

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Analysis Plan: 15FEB2021 Confidential

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Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Nervous system disorders	No. of Events (%)	189 (63.9)	137 (47.1)
	Median Survival Est. (95% CI)	2.83 (2.20, 3.68)	6.97 (3.94, NC)
	Hazard Ratio (95% CI) [a]		1.424 (1.140, 1.778)
	Treatment P-value [b]		0.00173
	Homogeneity P-value [c]		NA
Dizziness	No. of Events (%)	26 (8.8)	16 (5.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.506 (0.805, 2.816)
	Treatment P-value [b]		0.19689
	Homogeneity P-value [c]		NA

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Analysis Plan: 15FEB2021 Confidential

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Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Dysgeusia	No. of Events (%)	74 (25.0)	23 (7.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.412 (2.134, 5.457)
	Treatment P-value [b]		<.00001
	Homogeneity P-value [c]		NA
Headache	No. of Events (%)	10 (3.4)	17 (5.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.551 (0.251, 1.210)
	Treatment P-value [b]		0.13167
	Homogeneity P-value [c]		NA

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Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Neuropathy peripheral	No. of Events (%)	20 (6.8)	16 (5.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.178 (0.609, 2.277)
	Treatment P-value [b]		0.62573
	Homogeneity P-value [c]		NA
Paraesthesia	No. of Events (%)	15 (5.1)	8 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.757 (0.743, 4.157)
	Treatment P-value [b]		0.19358
	Homogeneity P-value [c]		NA

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Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Peripheral motor neuropathy	No. of Events (%)	11 (3.7)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00302
	Homogeneity P-value [c]		NA
Peripheral sensorimotor neuropathy	No. of Events (%)	8 (2.7)	2 (0.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.742 (0.794, 17.647)
	Treatment P-value [b]		0.07335
	Homogeneity P-value [c]		NA

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Analysis Plan: 15FEB2021 Confidential

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Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Peripheral sensory neuropathy	No. of Events (%)	102 (34.5)	66 (22.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.425 (1.043, 1.945)
	Treatment P-value [b]		0.02441
	Homogeneity P-value [c]		NA
Polyneuropathy	No. of Events (%)	5 (1.7)	6 (2.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.827 (0.252, 2.713)
	Treatment P-value [b]		0.75330
	Homogeneity P-value [c]		NA

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Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Taste disorder	No. of Events (%)	11 (3.7)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00084
	Homogeneity P-value [c]		NA
Psychiatric disorders	No. of Events (%)	55 (18.6)	46 (15.8)
	Median Survival Est. (95% CI)	NC (18.27, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.116 (0.753, 1.655)
	Treatment P-value [b]		0.58552
	Homogeneity P-value [c]		NA

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Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Anxiety	No. of Events (%)	8 (2.7)	6 (2.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.231 (0.426, 3.558)
	Treatment P-value [b]		0.70048
	Homogeneity P-value [c]		NA
Confusional state	No. of Events (%)	7 (2.4)	4 (1.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.614 (0.471, 5.528)
	Treatment P-value [b]		0.44161
	Homogeneity P-value [c]		NA

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Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Depression	No. of Events (%)	10 (3.4)	3 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.201 (0.880, 11.648)
	Treatment P-value [b]		0.06206
	Homogeneity P-value [c]		NA
Insomnia	No. of Events (%)	33 (11.1)	23 (7.9)
	Median Survival Est. (95% CI)	NC (18.27, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.332 (0.780, 2.275)
	Treatment P-value [b]		0.29230
	Homogeneity P-value [c]		NA

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Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Renal and urinary disorders	No. of Events (%)	75 (25.3)	52 (17.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.437 (1.008, 2.049)
	Treatment P-value [b]		0.04362
	Homogeneity P-value [c]		NA
Acute kidney injury	No. of Events (%)	19 (6.4)	8 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.337 (1.022, 5.344)
	Treatment P-value [b]		0.03822
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Analysis Plan: 15FEB2021 Confidential

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Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Dysuria	No. of Events (%)	11 (3.7)	4 (1.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.452 (0.775, 7.760)
	Treatment P-value [b]		0.11520
	Homogeneity P-value [c]		NA
Haematuria	No. of Events (%)	33 (11.1)	25 (8.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.265 (0.752, 2.130)
	Treatment P-value [b]		0.37400
	Homogeneity P-value [c]		NA

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Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Urinary retention	No. of Events (%)	5 (1.7)	5 (1.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.978 (0.283, 3.381)
	Treatment P-value [b]		0.97158
	Homogeneity P-value [c]		NA
Reproductive system and breast disorders	No. of Events (%)	10 (3.4)	12 (4.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.777 (0.335, 1.801)
	Treatment P-value [b]		0.55493
	Homogeneity P-value [c]		NA

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Analysis Plan: 15FEB2021 Confidential

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Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	101 (34.1)	68 (23.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.482 (1.088, 2.018)
	Treatment P-value [b]		0.01190
	Homogeneity P-value [c]		NA
Cough	No. of Events (%)	24 (8.1)	18 (6.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.180 (0.637, 2.184)
	Treatment P-value [b]		0.59821
	Homogeneity P-value [c]		NA

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Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Dysphonia	No. of Events (%)	8 (2.7)	2 (0.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.474 (0.730, 16.525)
	Treatment P-value [b]		0.09593
	Homogeneity P-value [c]		NA
Dyspnoea	No. of Events (%)	29 (9.8)	29 (10.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.930 (0.555, 1.558)
	Treatment P-value [b]		0.78322
	Homogeneity P-value [c]		NA

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Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Dyspnoea exertional	No. of Events (%)	8 (2.7)	3 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.312 (0.606, 8.819)
	Treatment P-value [b]		0.20734
	Homogeneity P-value [c]		NA
Epistaxis	No. of Events (%)	10 (3.4)	4 (1.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.416 (0.757, 7.713)
	Treatment P-value [b]		0.12420
	Homogeneity P-value [c]		NA

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Analysis Plan: 15FEB2021 Confidential

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Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Pulmonary embolism	No. of Events (%)	8 (2.7)	2 (0.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.620 (0.765, 17.121)
	Treatment P-value [b]		0.08283
	Homogeneity P-value [c]		NA
Rhinorrhoea	No. of Events (%)	14 (4.7)	7 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.835 (0.739, 4.559)
	Treatment P-value [b]		0.18433
	Homogeneity P-value [c]		NA

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Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Skin and subcutaneous tissue disorders	No. of Events (%)	237 (80.1)	150 (51.5)
	Median Survival Est. (95% CI)	0.66 (0.49, 0.79)	3.12 (1.41, NC)
	Hazard Ratio (95% CI) [a]		2.217 (1.800, 2.732)
	Treatment P-value [b]		<.00001
	Homogeneity P-value [c]		NA
Alopecia	No. of Events (%)	139 (47.0)	110 (37.8)
	Median Survival Est. (95% CI)	12.42 (2.40, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.113 (0.865, 1.431)
	Treatment P-value [b]		0.39527
	Homogeneity P-value [c]		NA

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Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Blister	No. of Events (%)	9 (3.0)	1 (0.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		8.901 (1.127, 70.273)
	Treatment P-value [b]		0.01202
	Homogeneity P-value [c]		NA
Drug eruption	No. of Events (%)	26 (8.8)	4 (1.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.765 (2.360, 19.394)
	Treatment P-value [b]		0.00004
	Homogeneity P-value [c]		NA

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Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Dry skin	No. of Events (%)	50 (16.9)	11 (3.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.639 (2.410, 8.928)
	Treatment P-value [b]		<.00001
	Homogeneity P-value [c]		NA
Erythema	No. of Events (%)	12 (4.1)	5 (1.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.360 (0.831, 6.699)
	Treatment P-value [b]		0.09645
	Homogeneity P-value [c]		NA

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Analysis Plan: 15FEB2021 Confidential

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Table TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Pruritus	No. of Events (%)	102 (34.5)	20 (6.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.363 (3.929, 10.304)
	Treatment P-value [b]		<.00001
	Homogeneity P-value [c]		NA
Rash	No. of Events (%)	50 (16.9)	17 (5.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.063 (1.765, 5.315)
	Treatment P-value [b]		0.00003
	Homogeneity P-value [c]		NA

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Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Rash erythematous	No. of Events (%)	10 (3.4)	1 (0.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.790 (1.252, 76.579)
	Treatment P-value [b]		0.00750
	Homogeneity P-value [c]		NA
Rash maculo-papular	No. of Events (%)	50 (16.9)	6 (2.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.396 (4.011, 22.011)
	Treatment P-value [b]		<.00001
	Homogeneity P-value [c]		NA

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Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Skin hyperpigmentation	No. of Events (%)	19 (6.4)	1 (0.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		20.704 (2.763, 155.151)
	Treatment P-value [b]		0.00003
	Homogeneity P-value [c]		NA
Vascular disorders	No. of Events (%)	43 (14.5)	37 (12.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.109 (0.713, 1.723)
	Treatment P-value [b]		0.64852
	Homogeneity P-value [c]		NA

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Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Hypertension	No. of Events (%)	11 (3.7)	10 (3.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.011 (0.427, 2.392)
	Treatment P-value [b]		0.98021
	Homogeneity P-value [c]		NA
Hypotension	No. of Events (%)	13 (4.4)	8 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.621 (0.671, 3.914)
	Treatment P-value [b]		0.28120
	Homogeneity P-value [c]		NA

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Table TEAE.KM.S1.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: <65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Any Event	No. of Events (%)	105 (99.1)	102 (99.0)
	Median Survival Est. (95% CI)	0.16 (0.13, 0.23)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.980 (0.746, 1.288)
	Treatment P-value [b]		0.94924
	Interaction P-value [c]		0.55868
Blood and lymphatic system disorders	No. of Events (%)	27 (25.5)	37 (35.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.602 (0.367, 0.989)
	Treatment P-value [b]		0.04573
	Interaction P-value [c]		0.84010

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Date/time of run: 20APR2021 13:50
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Subgroup: Age Group 1, Level: <65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Anaemia	No. of Events (%)	21 (19.8)	29 (28.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.626 (0.357, 1.098)
	Treatment P-value [b]		0.10506
	Interaction P-value [c]		0.96584
Febrile neutropenia	No. of Events (%)	0	5 (4.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.02154
	Interaction P-value [c]		0.98898

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Subgroup: Age Group 1, Level: <65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Eye disorders	No. of Events (%)	23 (21.7)	7 (6.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.288 (1.411, 7.662)
	Treatment P-value [b]		0.00330
	Interaction P-value [c]		0.96712
Dry eye	No. of Events (%)	7 (6.6)	2 (1.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.304 (0.686, 15.910)
	Treatment P-value [b]		0.10996
	Interaction P-value [c]		0.32583

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Subgroup: Age Group 1, Level: <65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Lacrimation increased	No. of Events (%)	10 (9.4)	2 (1.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.816 (1.055, 21.979)
	Treatment P-value [b]		0.02455
	Interaction P-value [c]		0.30398
Vision blurred	No. of Events (%)	2 (1.9)	3 (2.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.606 (0.101, 3.625)
	Treatment P-value [b]		0.58904
	Interaction P-value [c]		0.03844

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Subgroup: Age Group 1, Level: <65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Diarrhoea	No. of Events (%)	32 (30.2)	22 (21.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.425 (0.828, 2.452)
	Treatment P-value [b]		0.20376
	Interaction P-value [c]		0.68778
Dry mouth	No. of Events (%)	9 (8.5)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00262
	Interaction P-value [c]		0.98593

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Subgroup: Age Group 1, Level: <65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Chills	No. of Events (%)	4 (3.8)	1 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.876 (0.433, 34.677)
	Treatment P-value [b]		0.18785
	Interaction P-value [c]		0.74770
Fatigue	No. of Events (%)	35 (33.0)	22 (21.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.540 (0.904, 2.626)
	Treatment P-value [b]		0.11207
	Interaction P-value [c]		0.62262

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Analysis Plan: 15FEB2021 Confidential

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Subgroup: Age Group 1, Level: <65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Infections and infestations	No. of Events (%)	47 (44.3)	32 (31.1)
	Median Survival Est. (95% CI)	NC (3.88, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.460 (0.932, 2.288)
	Treatment P-value [b]		0.09068
	Interaction P-value [c]		0.81722
Conjunctivitis	No. of Events (%)	2 (1.9)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.17627
	Interaction P-value [c]		0.99213

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Subgroup: Age Group 1, Level: <65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Alanine aminotransferase increased	No. of Events (%)	8 (7.5)	1 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.896 (0.988, 63.128)
	Treatment P-value [b]		0.02007
	Interaction P-value [c]		0.68200
Aspartate aminotransferase increased	No. of Events (%)	11 (10.4)	2 (1.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.431 (1.204, 24.503)
	Treatment P-value [b]		0.01281
	Interaction P-value [c]		0.63543

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Subgroup: Age Group 1, Level: <65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Blood creatinine increased	No. of Events (%)	9 (8.5)	2 (1.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.377 (0.946, 20.257)
	Treatment P-value [b]		0.03830
	Interaction P-value [c]		0.79475
Neutrophil count decreased	No. of Events (%)	7 (6.6)	16 (15.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.374 (0.154, 0.910)
	Treatment P-value [b]		0.02932
	Interaction P-value [c]		0.34752

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Subgroup: Age Group 1, Level: <65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Weight decreased	No. of Events (%)	17 (16.0)	6 (5.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.719 (1.072, 6.897)
	Treatment P-value [b]		0.02909
	Interaction P-value [c]		0.78236
White blood cell count decreased	No. of Events (%)	3 (2.8)	11 (10.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.238 (0.066, 0.854)
	Treatment P-value [b]		0.01992
	Interaction P-value [c]		0.23428

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Subgroup: Age Group 1, Level: <65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Metabolism and nutrition disorders	No. of Events (%)	61 (57.5)	40 (38.8)
	Median Survival Est. (95% CI)	3.25 (1.58, NC)	NC (6.05, NC)
	Hazard Ratio (95% CI) [a]		1.577 (1.058, 2.350)
	Treatment P-value [b]		0.02256
	Interaction P-value [c]		0.57352
Decreased appetite	No. of Events (%)	44 (41.5)	25 (24.3)
	Median Survival Est. (95% CI)	NC (5.55, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.728 (1.058, 2.823)
	Treatment P-value [b]		0.02735
	Interaction P-value [c]		0.61973

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Subgroup: Age Group 1, Level: <65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Hyperglycaemia	No. of Events (%)	7 (6.6)	2 (1.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.367 (0.699, 16.207)
	Treatment P-value [b]		0.11120
	Interaction P-value [c]		0.51997
Musculoskeletal and connective tissue disorders	No. of Events (%)	34 (32.1)	48 (46.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	6.01 (2.56, NC)
	Hazard Ratio (95% CI) [a]		0.547 (0.352, 0.849)
	Treatment P-value [b]		0.00544
	Interaction P-value [c]		0.16283

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Subgroup: Age Group 1, Level: <65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Arthralgia	No. of Events (%)	8 (7.5)	14 (13.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.511 (0.214, 1.219)
	Treatment P-value [b]		0.11940
	Interaction P-value [c]		0.96568
Myalgia	No. of Events (%)	6 (5.7)	12 (11.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.452 (0.170, 1.205)
	Treatment P-value [b]		0.10202
	Interaction P-value [c]		0.92264

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Subgroup: Age Group 1, Level: <65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Nervous system disorders	No. of Events (%)	68 (64.2)	47 (45.6)
	Median Survival Est. (95% CI)	2.99 (2.00, 4.60)	8.84 (3.48, NC)
	Hazard Ratio (95% CI) [a]		1.476 (1.018, 2.141)
	Treatment P-value [b]		0.03394
	Interaction P-value [c]		0.92300
Dysgeusia	No. of Events (%)	27 (25.5)	9 (8.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.087 (1.452, 6.565)
	Treatment P-value [b]		0.00195
	Interaction P-value [c]		0.74200

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Astellas: 7465-CL-0301
Table TEAE.KM.S1.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: <65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Peripheral sensory neuropathy	No. of Events (%)	33 (31.1)	27 (26.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.053 (0.633, 1.751)
	Treatment P-value [b]		0.82087
	Interaction P-value [c]		0.11970
Renal and urinary disorders	No. of Events (%)	27 (25.5)	22 (21.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.210 (0.689, 2.125)
	Treatment P-value [b]		0.48431
	Interaction P-value [c]		0.42824

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S1.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: <65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Acute kidney injury	No. of Events (%)	8 (7.5)	4 (3.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.928 (0.581, 6.403)
	Treatment P-value [b]		0.27221
	Interaction P-value [c]		0.68351
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	30 (28.3)	20 (19.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.466 (0.833, 2.582)
	Treatment P-value [b]		0.18456
	Interaction P-value [c]		0.89876

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Subgroup: Age Group 1, Level: <65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Skin and subcutaneous tissue disorders	No. of Events (%)	88 (83.0)	53 (51.5)
	Median Survival Est. (95% CI)	0.69 (0.46, 0.92)	3.12 (0.72, NC)
	Hazard Ratio (95% CI) [a]		2.284 (1.622, 3.216)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.66920
Drug eruption	No. of Events (%)	7 (6.6)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00832
	Interaction P-value [c]		0.98787

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Table TEAE.KM.S1.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: <65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Dry skin	No. of Events (%)	18 (17.0)	6 (5.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.033 (1.204, 7.640)
	Treatment P-value [b]		0.01361
	Interaction P-value [c]		0.23604
Pruritus	No. of Events (%)	38 (35.8)	6 (5.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.419 (3.137, 17.546)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.55365

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Table TEAE.KM.S1.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: <65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Rash	No. of Events (%)	19 (17.9)	8 (7.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.411 (1.055, 5.508)
	Treatment P-value [b]		0.03200
	Interaction P-value [c]		0.47987
Rash maculo-papular	No. of Events (%)	19 (17.9)	2 (1.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.792 (2.281, 42.040)
	Treatment P-value [b]		0.00016
	Interaction P-value [c]		0.85000

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Subgroup: Age Group 1, Level: <65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Skin hyperpigmentation	No. of Events (%)	6 (5.7)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.01511
	Interaction P-value [c]		0.99102

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Table TEAE.KM.S1.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Any Event	No. of Events (%)	185 (97.4)	186 (98.9)
	Median Survival Est. (95% CI)	0.21 (0.16, 0.26)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.886 (0.722, 1.086)
	Treatment P-value [b]		0.21796
	Interaction P-value [c]		0.55868
Blood and lymphatic system disorders	No. of Events (%)	58 (30.5)	86 (45.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	12.94 (4.11, NC)
	Hazard Ratio (95% CI) [a]		0.566 (0.406, 0.790)
	Treatment P-value [b]		0.00068
	Interaction P-value [c]		0.84010

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Age Group 1, Level: >=65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Anaemia	No. of Events (%)	39 (20.5)	58 (30.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.617 (0.411, 0.925)
	Treatment P-value [b]		0.01786
	Interaction P-value [c]		0.96584
Febrile neutropenia	No. of Events (%)	4 (2.1)	11 (5.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.351 (0.112, 1.103)
	Treatment P-value [b]		0.05992
	Interaction P-value [c]		0.98898

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Subgroup: Age Group 1, Level: >=65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Eye disorders	No. of Events (%)	57 (30.0)	19 (10.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.357 (1.997, 5.643)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.96712
Dry eye	No. of Events (%)	12 (6.3)	1 (0.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		12.014 (1.563, 92.365)
	Treatment P-value [b]		0.00232
	Interaction P-value [c]		0.32583

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Subgroup: Age Group 1, Level: >=65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Lacrimation increased	No. of Events (%)	20 (10.5)	10 (5.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.977 (0.925, 4.224)
	Treatment P-value [b]		0.07114
	Interaction P-value [c]		0.30398
Vision blurred	No. of Events (%)	14 (7.4)	2 (1.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.045 (1.601, 31.003)
	Treatment P-value [b]		0.00264
	Interaction P-value [c]		0.03844

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Subgroup: Age Group 1, Level: >=65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Diarrhoea	No. of Events (%)	71 (37.4)	45 (23.9)
	Median Survival Est. (95% CI)	NC (15.11, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.631 (1.122, 2.370)
	Treatment P-value [b]		0.00970
	Interaction P-value [c]		0.68778
Dry mouth	No. of Events (%)	15 (7.9)	7 (3.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.166 (0.883, 5.312)
	Treatment P-value [b]		0.08546
	Interaction P-value [c]		0.98593

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Subgroup: Age Group 1, Level: >=65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Chills	No. of Events (%)	13 (6.8)	5 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.604 (0.928, 7.307)
	Treatment P-value [b]		0.05922
	Interaction P-value [c]		0.74770
Fatigue	No. of Events (%)	73 (38.4)	56 (29.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.313 (0.927, 1.860)
	Treatment P-value [b]		0.12266
	Interaction P-value [c]		0.62262

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Subgroup: Age Group 1, Level: >=65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Infections and infestations	No. of Events (%)	105 (55.3)	73 (38.8)
	Median Survival Est. (95% CI)	3.84 (2.86, 8.64)	NC (9.23, NC)
	Hazard Ratio (95% CI) [a]		1.556 (1.154, 2.098)
	Treatment P-value [b]		0.00331
	Interaction P-value [c]		0.81722
Conjunctivitis	No. of Events (%)	17 (8.9)	2 (1.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		8.616 (1.990, 37.299)
	Treatment P-value [b]		0.00050
	Interaction P-value [c]		0.99213

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Age Group 1, Level: >=65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Alanine aminotransferase increased	No. of Events (%)	19 (10.0)	4 (2.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.839 (1.646, 14.226)
	Treatment P-value [b]		0.00150
	Interaction P-value [c]		0.68200
Aspartate aminotransferase increased	No. of Events (%)	25 (13.2)	3 (1.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		8.651 (2.612, 28.655)
	Treatment P-value [b]		0.00002
	Interaction P-value [c]		0.63543

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Date/time of run: 20APR2021 13:50
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Astellas: 7465-CL-0301
Table TEAE.KM.S1.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Blood creatinine increased	No. of Events (%)	17 (8.9)	5 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.434 (1.267, 9.310)
	Treatment P-value [b]		0.01010
	Interaction P-value [c]		0.79475
Neutrophil count decreased	No. of Events (%)	26 (13.7)	38 (20.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.610 (0.370, 1.005)
	Treatment P-value [b]		0.04779
	Interaction P-value [c]		0.34752

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S1.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Weight decreased	No. of Events (%)	31 (16.3)	14 (7.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.321 (1.235, 4.363)
	Treatment P-value [b]		0.00706
	Interaction P-value [c]		0.78236
White blood cell count decreased	No. of Events (%)	13 (6.8)	21 (11.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.575 (0.288, 1.148)
	Treatment P-value [b]		0.11003
	Interaction P-value [c]		0.23428

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Analysis Plan: 15FEB2021 Confidential

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Table TEAE.KM.S1.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Metabolism and nutrition disorders	No. of Events (%)	113 (59.5)	86 (45.7)
	Median Survival Est. (95% CI)	1.91 (1.05, 4.86)	NC (2.79, NC)
	Hazard Ratio (95% CI) [a]		1.371 (1.035, 1.815)
	Treatment P-value [b]		0.02912
	Interaction P-value [c]		0.57352
Decreased appetite	No. of Events (%)	77 (40.5)	53 (28.2)
	Median Survival Est. (95% CI)	NC (9.10, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.483 (1.045, 2.105)
	Treatment P-value [b]		0.02650
	Interaction P-value [c]		0.61973

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S1.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Hyperglycaemia	No. of Events (%)	24 (12.6)	4 (2.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.271 (2.176, 18.075)
	Treatment P-value [b]		0.00010
	Interaction P-value [c]		0.51997
Musculoskeletal and connective tissue disorders	No. of Events (%)	66 (34.7)	72 (38.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.810 (0.580, 1.131)
	Treatment P-value [b]		0.22167
	Interaction P-value [c]		0.16283

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table TEAE.KM.S1.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Arthralgia	No. of Events (%)	12 (6.3)	22 (11.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.499 (0.247, 1.008)
	Treatment P-value [b]		0.04785
	Interaction P-value [c]		0.96568
Myalgia	No. of Events (%)	9 (4.7)	20 (10.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.425 (0.193, 0.933)
	Treatment P-value [b]		0.02860
	Interaction P-value [c]		0.92264

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Subgroup: Age Group 1, Level: >=65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Nervous system disorders	No. of Events (%)	121 (63.7)	90 (47.9)
	Median Survival Est. (95% CI)	2.79 (1.87, 3.81)	6.93 (2.79, NC)
	Hazard Ratio (95% CI) [a]		1.443 (1.098, 1.896)
	Treatment P-value [b]		0.00924
	Interaction P-value [c]		0.92300
Dysgeusia	No. of Events (%)	47 (24.7)	14 (7.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.629 (1.997, 6.591)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.74200

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Age Group 1, Level: >=65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Peripheral sensory neuropathy	No. of Events (%)	69 (36.3)	39 (20.7)
	Median Survival Est. (95% CI)	NC (10.58, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.754 (1.184, 2.598)
	Treatment P-value [b]		0.00440
	Interaction P-value [c]		0.11970
Renal and urinary disorders	No. of Events (%)	48 (25.3)	30 (16.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.622 (1.028, 2.560)
	Treatment P-value [b]		0.03590
	Interaction P-value [c]		0.42824

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table TEAE.KM.S1.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Acute kidney injury	No. of Events (%)	11 (5.8)	4 (2.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.722 (0.867, 8.552)
	Treatment P-value [b]		0.07167
	Interaction P-value [c]		0.68351
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	71 (37.4)	48 (25.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.532 (1.062, 2.209)
	Treatment P-value [b]		0.02093
	Interaction P-value [c]		0.89876

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table TEAE.KM.S1.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Skin and subcutaneous tissue disorders	No. of Events (%)	149 (78.4)	97 (51.6)
	Median Survival Est. (95% CI)	0.62 (0.43, 0.89)	3.25 (0.82, NC)
	Hazard Ratio (95% CI) [a]		2.081 (1.610, 2.691)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.66920
Drug eruption	No. of Events (%)	19 (10.0)	4 (2.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.817 (1.638, 14.159)
	Treatment P-value [b]		0.00159
	Interaction P-value [c]		0.98787

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Table TEAE.KM.S1.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Dry skin	No. of Events (%)	32 (16.8)	5 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.736 (2.624, 17.288)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.23604
Pruritus	No. of Events (%)	64 (33.7)	14 (7.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.423 (3.041, 9.672)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.55365

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Age Group 1, Level: >=65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Rash	No. of Events (%)	31 (16.3)	9 (4.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.598 (1.713, 7.558)
	Treatment P-value [b]		0.00028
	Interaction P-value [c]		0.47987
Rash maculo-papular	No. of Events (%)	31 (16.3)	4 (2.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		8.238 (2.908, 23.340)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.85000

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table TEAE.KM.S1.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Skin hyperpigmentation	No. of Events (%)	13 (6.8)	1 (0.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		13.448 (1.759, 102.803)
	Treatment P-value [b]		0.00108
	Interaction P-value [c]		0.99102

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
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Table TEAE.KM.S2.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Any Event	No. of Events (%)	241 (98.4)	224 (99.1)
	Median Survival Est. (95% CI)	0.20 (0.16, 0.23)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.920 (0.767, 1.105)
	Treatment P-value [b]		0.37336
	Interaction P-value [c]		0.93808
Blood and lymphatic system disorders	No. of Events (%)	69 (28.2)	91 (40.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (7.26, NC)
	Hazard Ratio (95% CI) [a]		0.593 (0.434, 0.812)
	Treatment P-value [b]		0.00091
	Interaction P-value [c]		0.82035

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S2.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Anaemia	No. of Events (%)	50 (20.4)	65 (28.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.642 (0.444, 0.928)
	Treatment P-value [b]		0.01672
	Interaction P-value [c]		0.72503
Febrile neutropenia	No. of Events (%)	4 (1.6)	10 (4.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.355 (0.111, 1.132)
	Treatment P-value [b]		0.06606
	Interaction P-value [c]		0.98869

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Astellas: 7465-CL-0301
Table TEAE.KM.S2.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Eye disorders	No. of Events (%)	61 (24.9)	18 (8.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.307 (1.955, 5.595)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.75919
Dry eye	No. of Events (%)	12 (4.9)	3 (1.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.588 (1.012, 12.717)
	Treatment P-value [b]		0.03428
	Interaction P-value [c]		0.98988

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Lacrimation increased	No. of Events (%)	26 (10.6)	7 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.381 (1.468, 7.790)
	Treatment P-value [b]		0.00246
	Interaction P-value [c]		0.14079
Vision blurred	No. of Events (%)	9 (3.7)	4 (1.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.985 (0.611, 6.448)
	Treatment P-value [b]		0.24537
	Interaction P-value [c]		0.18740

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Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Diarrhoea	No. of Events (%)	82 (33.5)	49 (21.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.572 (1.103, 2.239)
	Treatment P-value [b]		0.01168
	Interaction P-value [c]		0.94436
Dry mouth	No. of Events (%)	20 (8.2)	5 (2.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.728 (1.399, 9.935)
	Treatment P-value [b]		0.00470
	Interaction P-value [c]		0.74195

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Chills	No. of Events (%)	14 (5.7)	4 (1.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.229 (1.063, 9.811)
	Treatment P-value [b]		0.02883
	Interaction P-value [c]		0.64861
Fatigue	No. of Events (%)	84 (34.3)	59 (26.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.298 (0.930, 1.810)
	Treatment P-value [b]		0.12171
	Interaction P-value [c]		0.36383

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Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Infections and infestations	No. of Events (%)	123 (50.2)	76 (33.6)
	Median Survival Est. (95% CI)	7.82 (3.71, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.575 (1.183, 2.097)
	Treatment P-value [b]		0.00171
	Interaction P-value [c]		0.78793
Conjunctivitis	No. of Events (%)	14 (5.7)	1 (0.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		12.706 (1.671, 96.617)
	Treatment P-value [b]		0.00160
	Interaction P-value [c]		0.67772

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Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Alanine aminotransferase increased	No. of Events (%)	22 (9.0)	4 (1.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.119 (1.764, 14.854)
	Treatment P-value [b]		0.00079
	Interaction P-value [c]		0.80670
Amylase increased	No. of Events (%)	9 (3.7)	2 (0.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.980 (0.860, 18.423)
	Treatment P-value [b]		0.05546
	Interaction P-value [c]		0.99298

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Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Aspartate aminotransferase increased	No. of Events (%)	31 (12.7)	5 (2.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.857 (2.277, 15.064)
	Treatment P-value [b]		0.00003
	Interaction P-value [c]		0.98843
Blood creatinine increased	No. of Events (%)	23 (9.4)	5 (2.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.258 (1.618, 11.200)
	Treatment P-value [b]		0.00139
	Interaction P-value [c]		0.46893

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Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Neutrophil count decreased	No. of Events (%)	30 (12.2)	38 (16.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.648 (0.402, 1.046)
	Treatment P-value [b]		0.07774
	Interaction P-value [c]		0.10257
Weight decreased	No. of Events (%)	36 (14.7)	13 (5.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.561 (1.358, 4.828)
	Treatment P-value [b]		0.00257
	Interaction P-value [c]		0.99467

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Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
White blood cell count decreased	No. of Events (%)	14 (5.7)	24 (10.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.492 (0.254, 0.951)
	Treatment P-value [b]		0.03331
	Interaction P-value [c]		0.58044
Metabolism and nutrition disorders	No. of Events (%)	139 (56.7)	93 (41.2)
	Median Survival Est. (95% CI)	2.99 (1.77, 6.34)	NC (7.23, NC)
	Hazard Ratio (95% CI) [a]		1.422 (1.094, 1.850)
	Treatment P-value [b]		0.00751
	Interaction P-value [c]		0.59352

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Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Decreased appetite	No. of Events (%)	100 (40.8)	52 (23.0)
	Median Survival Est. (95% CI)	NC (9.10, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.819 (1.301, 2.544)
	Treatment P-value [b]		0.00037
	Interaction P-value [c]		0.11207
Hyperglycaemia	No. of Events (%)	22 (9.0)	4 (1.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.165 (1.780, 14.988)
	Treatment P-value [b]		0.00077
	Interaction P-value [c]		0.84329

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Musculoskeletal and connective tissue disorders	No. of Events (%)	80 (32.7)	95 (42.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (5.68, NC)
	Hazard Ratio (95% CI) [a]		0.647 (0.481, 0.872)
	Treatment P-value [b]		0.00411
	Interaction P-value [c]		0.22677
Arthralgia	No. of Events (%)	16 (6.5)	26 (11.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.522 (0.280, 0.974)
	Treatment P-value [b]		0.03783
	Interaction P-value [c]		0.88727

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Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Myalgia	No. of Events (%)	13 (5.3)	24 (10.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.470 (0.239, 0.922)
	Treatment P-value [b]		0.02375
	Interaction P-value [c]		0.62647
Nervous system disorders	No. of Events (%)	157 (64.1)	102 (45.1)
	Median Survival Est. (95% CI)	2.99 (2.20, 3.71)	7.66 (4.17, NC)
	Hazard Ratio (95% CI) [a]		1.521 (1.185, 1.953)
	Treatment P-value [b]		0.00070
	Interaction P-value [c]		0.52634

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Dysgeusia	No. of Events (%)	62 (25.3)	17 (7.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.585 (2.096, 6.131)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.71697
Peripheral motor neuropathy	No. of Events (%)	10 (4.1)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00453
	Interaction P-value [c]		0.99985

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Astellas: 7465-CL-0301
Table TEAE.KM.S2.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Peripheral sensory neuropathy	No. of Events (%)	85 (34.7)	53 (23.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.383 (0.981, 1.948)
	Treatment P-value [b]		0.06127
	Interaction P-value [c]		0.57962
Renal and urinary disorders	No. of Events (%)	64 (26.1)	43 (19.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.369 (0.930, 2.015)
	Treatment P-value [b]		0.10933
	Interaction P-value [c]		0.63684

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S2.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Acute kidney injury	No. of Events (%)	15 (6.1)	6 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.270 (0.881, 5.852)
	Treatment P-value [b]		0.08114
	Interaction P-value [c]		0.87019
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	82 (33.5)	59 (26.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.266 (0.906, 1.769)
	Treatment P-value [b]		0.16605
	Interaction P-value [c]		0.03107

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Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Skin and subcutaneous tissue disorders	No. of Events (%)	197 (80.4)	114 (50.4)
	Median Survival Est. (95% CI)	0.66 (0.49, 0.82)	3.12 (1.41, NC)
	Hazard Ratio (95% CI) [a]		2.205 (1.748, 2.780)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.66898
Blister	No. of Events (%)	9 (3.7)	1 (0.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.890 (0.999, 62.294)
	Treatment P-value [b]		0.02001
	Interaction P-value [c]		0.99949

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Table TEAE.KM.S2.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Drug eruption	No. of Events (%)	25 (10.2)	3 (1.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.872 (2.377, 26.071)
	Treatment P-value [b]		0.00006
	Interaction P-value [c]		0.23782
Dry skin	No. of Events (%)	40 (16.3)	9 (4.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.220 (2.048, 8.697)
	Treatment P-value [b]		0.00002
	Interaction P-value [c]		0.50949

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Table TEAE.KM.S2.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Pruritus	No. of Events (%)	82 (33.5)	17 (7.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.224 (3.098, 8.809)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.24940
Rash	No. of Events (%)	46 (18.8)	14 (6.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.193 (1.756, 5.809)
	Treatment P-value [b]		0.00006
	Interaction P-value [c]		0.46328

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Table TEAE.KM.S2.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Rash maculo-papular	No. of Events (%)	42 (17.1)	4 (1.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		10.238 (3.671, 28.553)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.53842
Skin hyperpigmentation	No. of Events (%)	14 (5.7)	1 (0.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		13.097 (1.722, 99.604)
	Treatment P-value [b]		0.00127
	Interaction P-value [c]		0.98914

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Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Any Event	No. of Events (%)	49 (96.1)	64 (98.5)
	Median Survival Est. (95% CI)	0.20 (0.13, 0.26)	0.13 (0.07, 0.23)
	Hazard Ratio (95% CI) [a]		0.905 (0.624, 1.314)
	Treatment P-value [b]		0.64142
	Interaction P-value [c]		0.93808
Blood and lymphatic system disorders	No. of Events (%)	16 (31.4)	32 (49.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	12.94 (1.41, NC)
	Hazard Ratio (95% CI) [a]		0.549 (0.301, 1.000)
	Treatment P-value [b]		0.05005
	Interaction P-value [c]		0.82035

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Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Anaemia	No. of Events (%)	10 (19.6)	22 (33.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (12.94, NC)
	Hazard Ratio (95% CI) [a]		0.552 (0.262, 1.167)
	Treatment P-value [b]		0.12061
	Interaction P-value [c]		0.72503
Febrile neutropenia	No. of Events (%)	0	6 (9.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.02741
	Interaction P-value [c]		0.98869

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Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Eye disorders	No. of Events (%)	19 (37.3)	8 (12.3)
	Median Survival Est. (95% CI)	NC (3.94, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.855 (1.687, 8.808)
	Treatment P-value [b]		0.00091
	Interaction P-value [c]		0.75919
Dry eye	No. of Events (%)	7 (13.7)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00217
	Interaction P-value [c]		0.98988

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Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Lacrimation increased	No. of Events (%)	4 (7.8)	5 (7.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.049 (0.282, 3.908)
	Treatment P-value [b]		0.91920
	Interaction P-value [c]		0.14079
Vision blurred	No. of Events (%)	7 (13.7)	1 (1.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		10.002 (1.230, 81.311)
	Treatment P-value [b]		0.00795
	Interaction P-value [c]		0.18740

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Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Diarrhoea	No. of Events (%)	21 (41.2)	18 (27.7)
	Median Survival Est. (95% CI)	NC (1.74, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.613 (0.859, 3.028)
	Treatment P-value [b]		0.12946
	Interaction P-value [c]		0.94436
Dry mouth	No. of Events (%)	4 (7.8)	2 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.682 (0.491, 14.647)
	Treatment P-value [b]		0.22255
	Interaction P-value [c]		0.74195

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Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Chills	No. of Events (%)	3 (5.9)	2 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.979 (0.331, 11.844)
	Treatment P-value [b]		0.45686
	Interaction P-value [c]		0.64861
Fatigue	No. of Events (%)	24 (47.1)	19 (29.2)
	Median Survival Est. (95% CI)	NC (1.35, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.785 (0.977, 3.259)
	Treatment P-value [b]		0.04767
	Interaction P-value [c]		0.36383

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Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Infections and infestations	No. of Events (%)	29 (56.9)	29 (44.6)
	Median Survival Est. (95% CI)	2.56 (1.84, NC)	NC (3.29, NC)
	Hazard Ratio (95% CI) [a]		1.453 (0.868, 2.432)
	Treatment P-value [b]		0.15528
	Interaction P-value [c]		0.78793
Conjunctivitis	No. of Events (%)	5 (9.8)	1 (1.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.791 (0.793, 58.159)
	Treatment P-value [b]		0.04221
	Interaction P-value [c]		0.67772

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Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Alanine aminotransferase increased	No. of Events (%)	5 (9.8)	1 (1.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.903 (0.807, 59.031)
	Treatment P-value [b]		0.04184
	Interaction P-value [c]		0.80670
Amylase increased	No. of Events (%)	2 (3.9)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.09426
	Interaction P-value [c]		0.99298

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table TEAE.KM.S2.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Aspartate aminotransferase increased	No. of Events (%)	5 (9.8)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00927
	Interaction P-value [c]		0.98843
Blood creatinine increased	No. of Events (%)	3 (5.9)	2 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.008 (0.336, 12.018)
	Treatment P-value [b]		0.43654
	Interaction P-value [c]		0.46893

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Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Neutrophil count decreased	No. of Events (%)	3 (5.9)	16 (24.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.215 (0.063, 0.739)
	Treatment P-value [b]		0.00792
	Interaction P-value [c]		0.10257
Weight decreased	No. of Events (%)	12 (23.5)	7 (10.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.570 (1.012, 6.531)
	Treatment P-value [b]		0.03773
	Interaction P-value [c]		0.99467

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Table TEAE.KM.S2.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
White blood cell count decreased	No. of Events (%)	2 (3.9)	8 (12.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.306 (0.065, 1.441)
	Treatment P-value [b]		0.11752
	Interaction P-value [c]		0.58044
Metabolism and nutrition disorders	No. of Events (%)	35 (68.6)	33 (50.8)
	Median Survival Est. (95% CI)	0.69 (0.46, 4.11)	5.29 (1.45, NC)
	Hazard Ratio (95% CI) [a]		1.649 (1.025, 2.655)
	Treatment P-value [b]		0.04715
	Interaction P-value [c]		0.59352

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Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Decreased appetite	No. of Events (%)	21 (41.2)	26 (40.0)
	Median Survival Est. (95% CI)	NC (2.14, NC)	NC (3.61, NC)
	Hazard Ratio (95% CI) [a]		1.060 (0.597, 1.885)
	Treatment P-value [b]		0.83503
	Interaction P-value [c]		0.11207
Hyperglycaemia	No. of Events (%)	9 (17.6)	2 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.235 (1.347, 28.860)
	Treatment P-value [b]		0.00736
	Interaction P-value [c]		0.84329

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Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Musculoskeletal and connective tissue disorders	No. of Events (%)	20 (39.2)	25 (38.5)
	Median Survival Est. (95% CI)	NC (3.42, NC)	NC (4.27, NC)
	Hazard Ratio (95% CI) [a]		0.972 (0.540, 1.751)
	Treatment P-value [b]		0.85004
	Interaction P-value [c]		0.22677
Arthralgia	No. of Events (%)	4 (7.8)	10 (15.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.475 (0.149, 1.514)
	Treatment P-value [b]		0.19459
	Interaction P-value [c]		0.88727

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Table TEAE.KM.S2.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Myalgia	No. of Events (%)	2 (3.9)	8 (12.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.309 (0.066, 1.453)
	Treatment P-value [b]		0.11487
	Interaction P-value [c]		0.62647
Nervous system disorders	No. of Events (%)	32 (62.7)	35 (53.8)
	Median Survival Est. (95% CI)	2.56 (0.95, 7.92)	2.86 (1.45, NC)
	Hazard Ratio (95% CI) [a]		1.277 (0.791, 2.064)
	Treatment P-value [b]		0.41575
	Interaction P-value [c]		0.52634

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Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Dysgeusia	No. of Events (%)	12 (23.5)	6 (9.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.915 (1.094, 7.770)
	Treatment P-value [b]		0.03073
	Interaction P-value [c]		0.71697
Peripheral motor neuropathy	No. of Events (%)	1 (2.0)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.24145
	Interaction P-value [c]		0.99985

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Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Peripheral sensory neuropathy	No. of Events (%)	17 (33.3)	13 (20.0)
	Median Survival Est. (95% CI)	NC (5.72, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.733 (0.842, 3.569)
	Treatment P-value [b]		0.13873
	Interaction P-value [c]		0.57962
Renal and urinary disorders	No. of Events (%)	11 (21.6)	9 (13.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.726 (0.715, 4.167)
	Treatment P-value [b]		0.21258
	Interaction P-value [c]		0.63684

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Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Acute kidney injury	No. of Events (%)	4 (7.8)	2 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.670 (0.489, 14.582)
	Treatment P-value [b]		0.23226
	Interaction P-value [c]		0.87019
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	19 (37.3)	9 (13.8)
	Median Survival Est. (95% CI)	NC (3.94, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.264 (1.476, 7.215)
	Treatment P-value [b]		0.00267
	Interaction P-value [c]		0.03107

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Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Skin and subcutaneous tissue disorders	No. of Events (%)	40 (78.4)	36 (55.4)
	Median Survival Est. (95% CI)	0.56 (0.30, 1.12)	2.86 (0.69, NC)
	Hazard Ratio (95% CI) [a]		1.974 (1.258, 3.099)
	Treatment P-value [b]		0.00395
	Interaction P-value [c]		0.66898
Blister	No. of Events (%)	0	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		NA
	Interaction P-value [c]		0.99949

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Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Drug eruption	No. of Events (%)	1 (2.0)	1 (1.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.277 (0.080, 20.423)
	Treatment P-value [b]		0.86783
	Interaction P-value [c]		0.23782
Dry skin	No. of Events (%)	10 (19.6)	2 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.431 (1.629, 33.903)
	Treatment P-value [b]		0.00253
	Interaction P-value [c]		0.50949

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Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Pruritus	No. of Events (%)	20 (39.2)	3 (4.6)
	Median Survival Est. (95% CI)	NC (0.92, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		11.355 (3.373, 38.222)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.24940
Rash	No. of Events (%)	4 (7.8)	3 (4.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.747 (0.391, 7.806)
	Treatment P-value [b]		0.45593
	Interaction P-value [c]		0.46328

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Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Rash maculo-papular	No. of Events (%)	8 (15.7)	2 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.714 (1.213, 26.913)
	Treatment P-value [b]		0.01551
	Interaction P-value [c]		0.53842
Skin hyperpigmentation	No. of Events (%)	5 (9.8)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00851
	Interaction P-value [c]		0.98914

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Table TEAE.KM.S3.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Any Event	No. of Events (%)	231 (98.7)	216 (98.6)
	Median Survival Est. (95% CI)	0.20 (0.16, 0.23)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.990 (0.821, 1.193)
	Treatment P-value [b]		0.99150
	Interaction P-value [c]		0.10014
Blood and lymphatic system disorders	No. of Events (%)	60 (25.6)	96 (43.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (5.36, NC)
	Hazard Ratio (95% CI) [a]		0.476 (0.345, 0.658)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.01525

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table TEAE.KM.S3.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Anaemia	No. of Events (%)	40 (17.1)	61 (27.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.555 (0.372, 0.827)
	Treatment P-value [b]		0.00313
	Interaction P-value [c]		0.23335
Febrile neutropenia	No. of Events (%)	2 (0.9)	15 (6.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.118 (0.027, 0.517)
	Treatment P-value [b]		0.00073
	Interaction P-value [c]		0.03720

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S3.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Eye disorders	No. of Events (%)	69 (29.5)	18 (8.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.927 (2.337, 6.597)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.12203
Dry eye	No. of Events (%)	15 (6.4)	2 (0.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.893 (1.576, 30.153)
	Treatment P-value [b]		0.00274
	Interaction P-value [c]		0.79671

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S3.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Lacrimation increased	No. of Events (%)	28 (12.0)	9 (4.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.872 (1.355, 6.087)
	Treatment P-value [b]		0.00399
	Interaction P-value [c]		0.19320
Vision blurred	No. of Events (%)	14 (6.0)	4 (1.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.182 (1.047, 9.668)
	Treatment P-value [b]		0.03129
	Interaction P-value [c]		0.83771

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Analysis Plan: 15FEB2021 Confidential

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Table TEAE.KM.S3.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Diarrhoea	No. of Events (%)	83 (35.5)	47 (21.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.703 (1.190, 2.436)
	Treatment P-value [b]		0.00300
	Interaction P-value [c]		0.34376
Dry mouth	No. of Events (%)	16 (6.8)	5 (2.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.019 (1.106, 8.242)
	Treatment P-value [b]		0.02145
	Interaction P-value [c]		0.60090

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Analysis Plan: 15FEB2021 Confidential

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Table TEAE.KM.S3.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Chills	No. of Events (%)	13 (5.6)	5 (2.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.438 (0.869, 6.839)
	Treatment P-value [b]		0.08006
	Interaction P-value [c]		0.59147
Fatigue	No. of Events (%)	88 (37.6)	55 (25.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.521 (1.086, 2.130)
	Treatment P-value [b]		0.01364
	Interaction P-value [c]		0.23290

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Analysis Plan: 15FEB2021 Confidential

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Table TEAE.KM.S3.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Infections and infestations	No. of Events (%)	123 (52.6)	81 (37.0)
	Median Survival Est. (95% CI)	4.76 (3.02, NC)	NC (10.41, NC)
	Hazard Ratio (95% CI) [a]		1.504 (1.136, 1.991)
	Treatment P-value [b]		0.00420
	Interaction P-value [c]		0.97278
Conjunctivitis	No. of Events (%)	14 (6.0)	2 (0.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.417 (1.458, 28.245)
	Treatment P-value [b]		0.00427
	Interaction P-value [c]		0.99134

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S3.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Alanine aminotransferase increased	No. of Events (%)	23 (9.8)	4 (1.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.466 (1.890, 15.807)
	Treatment P-value [b]		0.00042
	Interaction P-value [c]		0.92806
Amylase increased	No. of Events (%)	9 (3.8)	1 (0.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		8.129 (1.030, 64.173)
	Treatment P-value [b]		0.01811
	Interaction P-value [c]		0.45460

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Table TEAE.KM.S3.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Aspartate aminotransferase increased	No. of Events (%)	30 (12.8)	3 (1.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.652 (2.946, 31.629)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.34178
Blood creatinine increased	No. of Events (%)	17 (7.3)	5 (2.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.152 (1.163, 8.545)
	Treatment P-value [b]		0.01735
	Interaction P-value [c]		0.52017

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Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Neutrophil count decreased	No. of Events (%)	22 (9.4)	37 (16.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.496 (0.292, 0.840)
	Treatment P-value [b]		0.00841
	Interaction P-value [c]		0.49806
Weight decreased	No. of Events (%)	38 (16.2)	16 (7.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.276 (1.269, 4.082)
	Treatment P-value [b]		0.00442
	Interaction P-value [c]		0.65450

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Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
White blood cell count decreased	No. of Events (%)	12 (5.1)	18 (8.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.583 (0.281, 1.211)
	Treatment P-value [b]		0.14854
	Interaction P-value [c]		0.31778
Metabolism and nutrition disorders	No. of Events (%)	141 (60.3)	97 (44.3)
	Median Survival Est. (95% CI)	1.91 (1.35, 3.98)	NC (4.11, NC)
	Hazard Ratio (95% CI) [a]		1.415 (1.093, 1.834)
	Treatment P-value [b]		0.00773
	Interaction P-value [c]		0.91733

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Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Decreased appetite	No. of Events (%)	99 (42.3)	60 (27.4)
	Median Survival Est. (95% CI)	NC (6.37, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.565 (1.136, 2.157)
	Treatment P-value [b]		0.00541
	Interaction P-value [c]		0.88670
Hyperglycaemia	No. of Events (%)	28 (12.0)	4 (1.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.726 (2.359, 19.174)
	Treatment P-value [b]		0.00004
	Interaction P-value [c]		0.21570

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Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Musculoskeletal and connective tissue disorders	No. of Events (%)	79 (33.8)	87 (39.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (7.59, NC)
	Hazard Ratio (95% CI) [a]		0.754 (0.556, 1.022)
	Treatment P-value [b]		0.07175
	Interaction P-value [c]		0.36112
Arthralgia	No. of Events (%)	14 (6.0)	25 (11.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.482 (0.250, 0.927)
	Treatment P-value [b]		0.02755
	Interaction P-value [c]		0.73376

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Table TEAE.KM.S3.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Myalgia	No. of Events (%)	15 (6.4)	25 (11.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.531 (0.280, 1.007)
	Treatment P-value [b]		0.04724
	Interaction P-value [c]		0.98611
Nervous system disorders	No. of Events (%)	150 (64.1)	98 (44.7)
	Median Survival Est. (95% CI)	2.96 (2.27, 3.71)	8.61 (3.98, NC)
	Hazard Ratio (95% CI) [a]		1.586 (1.229, 2.046)
	Treatment P-value [b]		0.00029
	Interaction P-value [c]		0.18530

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Astellas: 7465-CL-0301
Table TEAE.KM.S3.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Dysgeusia	No. of Events (%)	60 (25.6)	18 (8.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.342 (1.973, 5.660)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.89670
Peripheral motor neuropathy	No. of Events (%)	11 (4.7)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00310
	Interaction P-value [c]		0.99756

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S3.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Peripheral sensory neuropathy	No. of Events (%)	81 (34.6)	49 (22.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.477 (1.036, 2.106)
	Treatment P-value [b]		0.02996
	Interaction P-value [c]		0.87930
Renal and urinary disorders	No. of Events (%)	61 (26.1)	41 (18.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.394 (0.938, 2.071)
	Treatment P-value [b]		0.09527
	Interaction P-value [c]		0.74721

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Table TEAE.KM.S3.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Acute kidney injury	No. of Events (%)	15 (6.4)	6 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.320 (0.900, 5.983)
	Treatment P-value [b]		0.06897
	Interaction P-value [c]		0.98911
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	80 (34.2)	53 (24.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.412 (0.998, 1.999)
	Treatment P-value [b]		0.04898
	Interaction P-value [c]		0.48987

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Table TEAE.KM.S3.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Skin and subcutaneous tissue disorders	No. of Events (%)	190 (81.2)	106 (48.4)
	Median Survival Est. (95% CI)	0.62 (0.46, 0.82)	5.13 (2.04, NC)
	Hazard Ratio (95% CI) [a]		2.446 (1.925, 3.107)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.03120
Drug eruption	No. of Events (%)	19 (8.1)	3 (1.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.038 (1.787, 20.401)
	Treatment P-value [b]		0.00095
	Interaction P-value [c]		0.79283

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Table TEAE.KM.S3.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Dry skin	No. of Events (%)	43 (18.4)	8 (3.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.298 (2.491, 11.268)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.43716
Pruritus	No. of Events (%)	80 (34.2)	12 (5.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.459 (4.065, 13.686)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.21071

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Table TEAE.KM.S3.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Rash	No. of Events (%)	44 (18.8)	13 (5.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.297 (1.776, 6.122)
	Treatment P-value [b]		0.00006
	Interaction P-value [c]		0.44032
Rash maculo-papular	No. of Events (%)	39 (16.7)	1 (0.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		38.851 (5.343, 282.519)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.02131

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Table TEAE.KM.S3.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Skin hyperpigmentation	No. of Events (%)	16 (6.8)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00009
	Interaction P-value [c]		0.99071

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Table TEAE.KM.S3.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Any Event	No. of Events (%)	59 (95.2)	72 (100.0)
	Median Survival Est. (95% CI)	0.20 (0.13, 0.26)	0.13 (0.10, 0.20)
	Hazard Ratio (95% CI) [a]		0.711 (0.503, 1.005)
	Treatment P-value [b]		0.06855
	Interaction P-value [c]		0.10014
Blood and lymphatic system disorders	No. of Events (%)	25 (40.3)	27 (37.5)
	Median Survival Est. (95% CI)	NC (4.86, NC)	NC (5.68, NC)
	Hazard Ratio (95% CI) [a]		1.042 (0.605, 1.796)
	Treatment P-value [b]		0.86871
	Interaction P-value [c]		0.01525

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Table TEAE.KM.S3.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Anaemia	No. of Events (%)	20 (32.3)	26 (36.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (7.26, NC)
	Hazard Ratio (95% CI) [a]		0.853 (0.476, 1.527)
	Treatment P-value [b]		0.58195
	Interaction P-value [c]		0.23335
Febrile neutropenia	No. of Events (%)	2 (3.2)	1 (1.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.362 (0.214, 26.051)
	Treatment P-value [b]		0.44672
	Interaction P-value [c]		0.03720

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Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Eye disorders	No. of Events (%)	11 (17.7)	8 (11.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.718 (0.691, 4.270)
	Treatment P-value [b]		0.24465
	Interaction P-value [c]		0.12203
Dry eye	No. of Events (%)	4 (6.5)	1 (1.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.871 (0.544, 43.583)
	Treatment P-value [b]		0.11911
	Interaction P-value [c]		0.79671

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Table TEAE.KM.S3.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Lacrimation increased	No. of Events (%)	2 (3.2)	3 (4.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.792 (0.132, 4.739)
	Treatment P-value [b]		0.80580
	Interaction P-value [c]		0.19320
Vision blurred	No. of Events (%)	2 (3.2)	1 (1.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.413 (0.219, 26.613)
	Treatment P-value [b]		0.46448
	Interaction P-value [c]		0.83771

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Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Diarrhoea	No. of Events (%)	20 (32.3)	20 (27.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.205 (0.648, 2.240)
	Treatment P-value [b]		0.59619
	Interaction P-value [c]		0.34376
Dry mouth	No. of Events (%)	8 (12.9)	2 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.942 (1.049, 23.272)
	Treatment P-value [b]		0.02362
	Interaction P-value [c]		0.60090

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Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Chills	No. of Events (%)	4 (6.5)	1 (1.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.731 (0.529, 42.305)
	Treatment P-value [b]		0.11619
	Interaction P-value [c]		0.59147
Fatigue	No. of Events (%)	20 (32.3)	23 (31.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.001 (0.550, 1.822)
	Treatment P-value [b]		0.96995
	Interaction P-value [c]		0.23290

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Table TEAE.KM.S3.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Infections and infestations	No. of Events (%)	29 (46.8)	24 (33.3)
	Median Survival Est. (95% CI)	8.64 (3.09, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.520 (0.885, 2.611)
	Treatment P-value [b]		0.12528
	Interaction P-value [c]		0.97278
Conjunctivitis	No. of Events (%)	5 (8.1)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.01159
	Interaction P-value [c]		0.99134

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Astellas: 7465-CL-0301
Table TEAE.KM.S3.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Alanine aminotransferase increased	No. of Events (%)	4 (6.5)	1 (1.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.886 (0.546, 43.716)
	Treatment P-value [b]		0.12075
	Interaction P-value [c]		0.92806
Amylase increased	No. of Events (%)	2 (3.2)	1 (1.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.428 (0.220, 26.780)
	Treatment P-value [b]		0.47028
	Interaction P-value [c]		0.45460

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Astellas: 7465-CL-0301
Table TEAE.KM.S3.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Aspartate aminotransferase increased	No. of Events (%)	6 (9.7)	2 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.672 (0.741, 18.195)
	Treatment P-value [b]		0.08996
	Interaction P-value [c]		0.34178
Blood creatinine increased	No. of Events (%)	9 (14.5)	2 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.743 (1.241, 26.582)
	Treatment P-value [b]		0.01169
	Interaction P-value [c]		0.52017

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Table TEAE.KM.S3.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Neutrophil count decreased	No. of Events (%)	11 (17.7)	17 (23.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.682 (0.319, 1.456)
	Treatment P-value [b]		0.33381
	Interaction P-value [c]		0.49806
Weight decreased	No. of Events (%)	10 (16.1)	4 (5.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.062 (0.960, 9.762)
	Treatment P-value [b]		0.04737
	Interaction P-value [c]		0.65450

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Table TEAE.KM.S3.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
White blood cell count decreased	No. of Events (%)	4 (6.5)	14 (19.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.296 (0.097, 0.900)
	Treatment P-value [b]		0.02406
	Interaction P-value [c]		0.31778
Metabolism and nutrition disorders	No. of Events (%)	33 (53.2)	29 (40.3)
	Median Survival Est. (95% CI)	5.06 (1.25, NC)	NC (3.61, NC)
	Hazard Ratio (95% CI) [a]		1.458 (0.885, 2.401)
	Treatment P-value [b]		0.15061
	Interaction P-value [c]		0.91733

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Table TEAE.KM.S3.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Decreased appetite	No. of Events (%)	22 (35.5)	18 (25.0)
	Median Survival Est. (95% CI)	NC (7.52, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.487 (0.798, 2.773)
	Treatment P-value [b]		0.21469
	Interaction P-value [c]		0.88670
Hyperglycaemia	No. of Events (%)	3 (4.8)	2 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.815 (0.303, 10.864)
	Treatment P-value [b]		0.50099
	Interaction P-value [c]		0.21570

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Table TEAE.KM.S3.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Musculoskeletal and connective tissue disorders	No. of Events (%)	21 (33.9)	33 (45.8)
	Median Survival Est. (95% CI)	NC (6.60, NC)	NC (1.58, NC)
	Hazard Ratio (95% CI) [a]		0.563 (0.326, 0.973)
	Treatment P-value [b]		0.04506
	Interaction P-value [c]		0.36112
Arthralgia	No. of Events (%)	6 (9.7)	11 (15.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.592 (0.219, 1.602)
	Treatment P-value [b]		0.30588
	Interaction P-value [c]		0.73376

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Table TEAE.KM.S3.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Myalgia	No. of Events (%)	0	7 (9.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.01247
	Interaction P-value [c]		0.98611
Nervous system disorders	No. of Events (%)	39 (62.9)	39 (54.2)
	Median Survival Est. (95% CI)	2.73 (1.45, 4.14)	2.40 (0.85, NC)
	Hazard Ratio (95% CI) [a]		1.122 (0.719, 1.749)
	Treatment P-value [b]		0.68433
	Interaction P-value [c]		0.18530

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Table TEAE.KM.S3.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Dysgeusia	No. of Events (%)	14 (22.6)	5 (6.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.606 (1.299, 10.014)
	Treatment P-value [b]		0.00956
	Interaction P-value [c]		0.89670
Peripheral motor neuropathy	No. of Events (%)	0	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		NA
	Interaction P-value [c]		0.99756

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Table TEAE.KM.S3.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Peripheral sensory neuropathy	No. of Events (%)	21 (33.9)	17 (23.6)
	Median Survival Est. (95% CI)	NC (5.72, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.396 (0.736, 2.646)
	Treatment P-value [b]		0.28312
	Interaction P-value [c]		0.87930
Renal and urinary disorders	No. of Events (%)	14 (22.6)	11 (15.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.612 (0.732, 3.551)
	Treatment P-value [b]		0.22871
	Interaction P-value [c]		0.74721

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Table TEAE.KM.S3.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Acute kidney injury	No. of Events (%)	4 (6.5)	2 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.352 (0.431, 12.839)
	Treatment P-value [b]		0.28953
	Interaction P-value [c]		0.98911
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	21 (33.9)	15 (20.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.838 (0.948, 3.567)
	Treatment P-value [b]		0.06292
	Interaction P-value [c]		0.48987

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Table TEAE.KM.S3.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Skin and subcutaneous tissue disorders	No. of Events (%)	47 (75.8)	44 (61.1)
	Median Survival Est. (95% CI)	0.72 (0.39, 1.08)	0.69 (0.66, 7.62)
	Hazard Ratio (95% CI) [a]		1.451 (0.961, 2.189)
	Treatment P-value [b]		0.07657
	Interaction P-value [c]		0.03120
Drug eruption	No. of Events (%)	7 (11.3)	1 (1.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		8.354 (1.028, 67.879)
	Treatment P-value [b]		0.01800
	Interaction P-value [c]		0.79283

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Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Dry skin	No. of Events (%)	7 (11.3)	3 (4.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.867 (0.741, 11.087)
	Treatment P-value [b]		0.11883
	Interaction P-value [c]		0.43716
Pruritus	No. of Events (%)	22 (35.5)	8 (11.1)
	Median Survival Est. (95% CI)	NC (7.92, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.910 (1.740, 8.785)
	Treatment P-value [b]		0.00044
	Interaction P-value [c]		0.21071

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Table TEAE.KM.S3.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Rash	No. of Events (%)	6 (9.7)	4 (5.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.893 (0.534, 6.710)
	Treatment P-value [b]		0.32660
	Interaction P-value [c]		0.44032
Rash maculo-papular	No. of Events (%)	11 (17.7)	5 (6.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.770 (0.962, 7.972)
	Treatment P-value [b]		0.04920
	Interaction P-value [c]		0.02131

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Table TEAE.KM.S3.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Skin hyperpigmentation	No. of Events (%)	3 (4.8)	1 (1.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.602 (0.375, 34.631)
	Treatment P-value [b]		0.23799
	Interaction P-value [c]		0.99071

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Astellas: 7465-CL-0301
Table TEAE.KM.S4.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Western Europe

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Any Event	No. of Events (%)	118 (96.7)	121 (98.4)
	Median Survival Est. (95% CI)	0.23 (0.16, 0.26)	0.13 (0.07, 0.16)
	Hazard Ratio (95% CI) [a]		0.857 (0.665, 1.105)
	Treatment P-value [b]		0.32375
	Interaction P-value [c]		0.68127
Blood and lymphatic system disorders	No. of Events (%)	31 (25.4)	52 (42.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (2.33, NC)
	Hazard Ratio (95% CI) [a]		0.478 (0.307, 0.747)
	Treatment P-value [b]		0.00084
	Interaction P-value [c]		0.05004

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S4.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Western Europe

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Anaemia	No. of Events (%)	21 (17.2)	38 (30.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.485 (0.285, 0.827)
	Treatment P-value [b]		0.00528
	Interaction P-value [c]		0.00445
Febrile neutropenia	No. of Events (%)	0	6 (4.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.01257
	Interaction P-value [c]		0.99987

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Table TEAE.KM.S4.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Western Europe

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Eye disorders	No. of Events (%)	42 (34.4)	7 (5.7)
	Median Survival Est. (95% CI)	NC (8.80, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.944 (3.119, 15.462)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.04826
Lacrimation increased	No. of Events (%)	18 (14.8)	3 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.159 (1.814, 20.909)
	Treatment P-value [b]		0.00094
	Interaction P-value [c]		0.11050

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Table TEAE.KM.S4.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Western Europe

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Vision blurred	No. of Events (%)	9 (7.4)	1 (0.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		8.748 (1.108, 69.053)
	Treatment P-value [b]		0.01357
	Interaction P-value [c]		0.34487
Diarrhoea	No. of Events (%)	51 (41.8)	24 (19.5)
	Median Survival Est. (95% CI)	NC (5.68, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.359 (1.452, 3.832)
	Treatment P-value [b]		0.00038
	Interaction P-value [c]		0.02358

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Table TEAE.KM.S4.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Western Europe

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Dry mouth	No. of Events (%)	10 (8.2)	5 (4.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.002 (0.684, 5.858)
	Treatment P-value [b]		0.19556
	Interaction P-value [c]		0.85466
Chills	No. of Events (%)	5 (4.1)	1 (0.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.980 (0.582, 42.632)
	Treatment P-value [b]		0.10921
	Interaction P-value [c]		0.41717

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Table TEAE.KM.S4.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Western Europe

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Fatigue	No. of Events (%)	43 (35.2)	34 (27.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.276 (0.814, 2.000)
	Treatment P-value [b]		0.28840
	Interaction P-value [c]		0.26690
Infections and infestations	No. of Events (%)	64 (52.5)	53 (43.1)
	Median Survival Est. (95% CI)	4.14 (2.86, NC)	NC (4.34, NC)
	Hazard Ratio (95% CI) [a]		1.242 (0.863, 1.788)
	Treatment P-value [b]		0.23848
	Interaction P-value [c]		0.19322

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Subgroup: Region, Level: Western Europe

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Conjunctivitis	No. of Events (%)	13 (10.7)	1 (0.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		13.038 (1.706, 99.669)
	Treatment P-value [b]		0.00133
	Interaction P-value [c]		0.32369
Alanine aminotransferase increased	No. of Events (%)	10 (8.2)	2 (1.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.982 (1.092, 22.740)
	Treatment P-value [b]		0.02239
	Interaction P-value [c]		0.47337

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Table TEAE.KM.S4.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Western Europe

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Aspartate aminotransferase increased	No. of Events (%)	14 (11.5)	1 (0.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		14.013 (1.843, 106.556)
	Treatment P-value [b]		0.00079
	Interaction P-value [c]		0.68299
Blood creatinine increased	No. of Events (%)	8 (6.6)	3 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.624 (0.696, 9.890)
	Treatment P-value [b]		0.13351
	Interaction P-value [c]		0.82290

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Table TEAE.KM.S4.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Western Europe

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Neutrophil count decreased	No. of Events (%)	4 (3.3)	12 (9.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.313 (0.101, 0.971)
	Treatment P-value [b]		0.02266
	Interaction P-value [c]		0.61418
Weight decreased	No. of Events (%)	15 (12.3)	9 (7.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.638 (0.717, 3.744)
	Treatment P-value [b]		0.24586
	Interaction P-value [c]		0.50575

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Subgroup: Region, Level: Western Europe

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
White blood cell count decreased	No. of Events (%)	1 (0.8)	6 (4.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.159 (0.019, 1.322)
	Treatment P-value [b]		0.04432
	Interaction P-value [c]		0.26977
Metabolism and nutrition disorders	No. of Events (%)	63 (51.6)	53 (43.1)
	Median Survival Est. (95% CI)	4.07 (2.10, NC)	NC (2.79, NC)
	Hazard Ratio (95% CI) [a]		1.125 (0.780, 1.621)
	Treatment P-value [b]		0.50401
	Interaction P-value [c]		0.15788

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Subgroup: Region, Level: Western Europe

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Decreased appetite	No. of Events (%)	41 (33.6)	35 (28.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.106 (0.705, 1.737)
	Treatment P-value [b]		0.64806
	Interaction P-value [c]		0.12069
Hyperglycaemia	No. of Events (%)	15 (12.3)	4 (3.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.766 (1.250, 11.349)
	Treatment P-value [b]		0.01103
	Interaction P-value [c]		0.98065

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Subgroup: Region, Level: Western Europe

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Musculoskeletal and connective tissue disorders	No. of Events (%)	48 (39.3)	54 (43.9)
	Median Survival Est. (95% CI)	NC (6.31, NC)	8.02 (3.02, NC)
	Hazard Ratio (95% CI) [a]		0.784 (0.532, 1.157)
	Treatment P-value [b]		0.21063
	Interaction P-value [c]		0.55162
Arthralgia	No. of Events (%)	11 (9.0)	14 (11.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.742 (0.337, 1.635)
	Treatment P-value [b]		0.44659
	Interaction P-value [c]		0.41958

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Subgroup: Region, Level: Western Europe

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Myalgia	No. of Events (%)	11 (9.0)	13 (10.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.807 (0.361, 1.801)
	Treatment P-value [b]		0.57513
	Interaction P-value [c]		0.10858
Nervous system disorders	No. of Events (%)	74 (60.7)	48 (39.0)
	Median Survival Est. (95% CI)	2.79 (2.00, 3.81)	NC (6.97, NC)
	Hazard Ratio (95% CI) [a]		1.770 (1.230, 2.547)
	Treatment P-value [b]		0.00187
	Interaction P-value [c]		0.33276

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Subgroup: Region, Level: Western Europe

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Dysgeusia	No. of Events (%)	24 (19.7)	6 (4.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.267 (1.745, 10.436)
	Treatment P-value [b]		0.00055
	Interaction P-value [c]		0.40176
Peripheral sensory neuropathy	No. of Events (%)	36 (29.5)	13 (10.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.883 (1.529, 5.436)
	Treatment P-value [b]		0.00063
	Interaction P-value [c]		0.02158

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Date/time of run: 20APR2021 13:50
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Table TEAE.KM.S4.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Western Europe

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Renal and urinary disorders	No. of Events (%)	32 (26.2)	19 (15.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.702 (0.965, 3.003)
	Treatment P-value [b]		0.06596
	Interaction P-value [c]		0.71056
Acute kidney injury	No. of Events (%)	9 (7.4)	3 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.917 (0.790, 10.774)
	Treatment P-value [b]		0.09400
	Interaction P-value [c]		0.81987

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S4.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Western Europe

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	36 (29.5)	27 (22.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.327 (0.806, 2.186)
	Treatment P-value [b]		0.26620
	Interaction P-value [c]		0.23510
Skin and subcutaneous tissue disorders	No. of Events (%)	88 (72.1)	48 (39.0)
	Median Survival Est. (95% CI)	1.05 (0.82, 1.18)	NC (3.12, NC)
	Hazard Ratio (95% CI) [a]		2.379 (1.672, 3.384)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.33244

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Subgroup: Region, Level: Western Europe

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Drug eruption	No. of Events (%)	4 (3.3)	1 (0.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.962 (0.443, 35.449)
	Treatment P-value [b]		0.18411
	Interaction P-value [c]		0.94205
Dry skin	No. of Events (%)	21 (17.2)	1 (0.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		21.866 (2.941, 162.555)
	Treatment P-value [b]		0.00001
	Interaction P-value [c]		0.12778

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Table TEAE.KM.S4.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Western Europe

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Pruritus	No. of Events (%)	28 (23.0)	2 (1.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		15.470 (3.685, 64.940)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.24829
Rash	No. of Events (%)	29 (23.8)	4 (3.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.864 (2.764, 22.371)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.02195

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Subgroup: Region, Level: Western Europe

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Rash maculo-papular	No. of Events (%)	10 (8.2)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00157
	Interaction P-value [c]		0.98747
Skin hyperpigmentation	No. of Events (%)	2 (1.6)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.16308
	Interaction P-value [c]		0.99993

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Subgroup: Region, Level: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Any Event	No. of Events (%)	41 (97.6)	39 (100.0)
	Median Survival Est. (95% CI)	0.26 (0.13, 0.26)	0.10 (0.07, 0.20)
	Hazard Ratio (95% CI) [a]		0.870 (0.560, 1.350)
	Treatment P-value [b]		0.39603
	Interaction P-value [c]		0.68127
Blood and lymphatic system disorders	No. of Events (%)	10 (23.8)	22 (56.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	2.79 (0.72, NC)
	Hazard Ratio (95% CI) [a]		0.316 (0.149, 0.667)
	Treatment P-value [b]		0.00178
	Interaction P-value [c]		0.05004

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Subgroup: Region, Level: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Anaemia	No. of Events (%)	5 (11.9)	18 (46.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (1.38, NC)
	Hazard Ratio (95% CI) [a]		0.197 (0.073, 0.530)
	Treatment P-value [b]		0.00061
	Interaction P-value [c]		0.00445
Febrile neutropenia	No. of Events (%)	1 (2.4)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.33523
	Interaction P-value [c]		0.99987

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Subgroup: Region, Level: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Eye disorders	No. of Events (%)	16 (38.1)	9 (23.1)
	Median Survival Est. (95% CI)	NC (3.94, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.885 (0.833, 4.266)
	Treatment P-value [b]		0.10991
	Interaction P-value [c]		0.04826
Lacrimation increased	No. of Events (%)	6 (14.3)	5 (12.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.120 (0.342, 3.669)
	Treatment P-value [b]		0.82930
	Interaction P-value [c]		0.11050

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Subgroup: Region, Level: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Vision blurred	No. of Events (%)	3 (7.1)	1 (2.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.769 (0.288, 26.619)
	Treatment P-value [b]		0.36367
	Interaction P-value [c]		0.34487
Diarrhoea	No. of Events (%)	13 (31.0)	16 (41.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (2.69, NC)
	Hazard Ratio (95% CI) [a]		0.702 (0.338, 1.460)
	Treatment P-value [b]		0.36814
	Interaction P-value [c]		0.02358

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Subgroup: Region, Level: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Dry mouth	No. of Events (%)	7 (16.7)	2 (5.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.450 (0.717, 16.607)
	Treatment P-value [b]		0.09999
	Interaction P-value [c]		0.85466
Chills	No. of Events (%)	5 (11.9)	5 (12.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.935 (0.271, 3.231)
	Treatment P-value [b]		0.91152
	Interaction P-value [c]		0.41717

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Subgroup: Region, Level: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Fatigue	No. of Events (%)	19 (45.2)	18 (46.2)
	Median Survival Est. (95% CI)	NC (1.48, NC)	8.08 (2.10, NC)
	Hazard Ratio (95% CI) [a]		0.933 (0.490, 1.778)
	Treatment P-value [b]		0.83217
	Interaction P-value [c]		0.26690
Infections and infestations	No. of Events (%)	26 (61.9)	13 (33.3)
	Median Survival Est. (95% CI)	3.45 (1.28, NC)	NC (5.39, NC)
	Hazard Ratio (95% CI) [a]		2.465 (1.266, 4.798)
	Treatment P-value [b]		0.00790
	Interaction P-value [c]		0.19322

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Subgroup: Region, Level: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Conjunctivitis	No. of Events (%)	1 (2.4)	1 (2.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.935 (0.059, 14.956)
	Treatment P-value [b]		0.95956
	Interaction P-value [c]		0.32369
Alanine aminotransferase increased	No. of Events (%)	5 (11.9)	2 (5.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.421 (0.470, 12.482)
	Treatment P-value [b]		0.27678
	Interaction P-value [c]		0.47337

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Subgroup: Region, Level: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Aspartate aminotransferase increased	No. of Events (%)	9 (21.4)	2 (5.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.514 (0.975, 20.896)
	Treatment P-value [b]		0.03132
	Interaction P-value [c]		0.68299
Blood creatinine increased	No. of Events (%)	9 (21.4)	2 (5.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.536 (0.980, 20.996)
	Treatment P-value [b]		0.03441
	Interaction P-value [c]		0.82290

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Astellas: 7465-CL-0301
Table TEAE.KM.S4.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Neutrophil count decreased	No. of Events (%)	6 (14.3)	8 (20.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.620 (0.215, 1.787)
	Treatment P-value [b]		0.38278
	Interaction P-value [c]		0.61418
Weight decreased	No. of Events (%)	12 (28.6)	4 (10.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.037 (0.979, 9.417)
	Treatment P-value [b]		0.04841
	Interaction P-value [c]		0.50575

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Astellas: 7465-CL-0301
Table TEAE.KM.S4.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
White blood cell count decreased	No. of Events (%)	4 (9.5)	3 (7.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.200 (0.269, 5.363)
	Treatment P-value [b]		0.80009
	Interaction P-value [c]		0.26977
Metabolism and nutrition disorders	No. of Events (%)	30 (71.4)	23 (59.0)
	Median Survival Est. (95% CI)	0.90 (0.46, 2.17)	1.74 (0.69, NC)
	Hazard Ratio (95% CI) [a]		1.356 (0.787, 2.335)
	Treatment P-value [b]		0.28738
	Interaction P-value [c]		0.15788

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Table TEAE.KM.S4.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Decreased appetite	No. of Events (%)	19 (45.2)	12 (30.8)
	Median Survival Est. (95% CI)	NC (2.10, NC)	NC (7.23, NC)
	Hazard Ratio (95% CI) [a]		1.534 (0.745, 3.162)
	Treatment P-value [b]		0.27612
	Interaction P-value [c]		0.12069
Hyperglycaemia	No. of Events (%)	7 (16.7)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00782
	Interaction P-value [c]		0.98065

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Table TEAE.KM.S4.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Musculoskeletal and connective tissue disorders	No. of Events (%)	14 (33.3)	21 (53.8)
	Median Survival Est. (95% CI)	NC (3.48, NC)	2.56 (0.62, NC)
	Hazard Ratio (95% CI) [a]		0.508 (0.258, 0.999)
	Treatment P-value [b]		0.05629
	Interaction P-value [c]		0.55162
Arthralgia	No. of Events (%)	3 (7.1)	8 (20.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.309 (0.082, 1.165)
	Treatment P-value [b]		0.06925
	Interaction P-value [c]		0.41958

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Table TEAE.KM.S4.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Myalgia	No. of Events (%)	1 (2.4)	3 (7.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.303 (0.032, 2.914)
	Treatment P-value [b]		0.27552
	Interaction P-value [c]		0.10858
Nervous system disorders	No. of Events (%)	30 (71.4)	24 (61.5)
	Median Survival Est. (95% CI)	1.87 (0.95, 4.21)	2.79 (1.15, 6.93)
	Hazard Ratio (95% CI) [a]		1.147 (0.671, 1.963)
	Treatment P-value [b]		0.65160
	Interaction P-value [c]		0.33276

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Table TEAE.KM.S4.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Dysgeusia	No. of Events (%)	14 (33.3)	7 (17.9)
	Median Survival Est. (95% CI)	NC (5.55, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.952 (0.788, 4.837)
	Treatment P-value [b]		0.14837
	Interaction P-value [c]		0.40176
Peripheral sensory neuropathy	No. of Events (%)	16 (38.1)	10 (25.6)
	Median Survival Est. (95% CI)	NC (4.17, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.500 (0.681, 3.306)
	Treatment P-value [b]		0.30103
	Interaction P-value [c]		0.02158

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Table TEAE.KM.S4.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Renal and urinary disorders	No. of Events (%)	14 (33.3)	9 (23.1)
	Median Survival Est. (95% CI)	NC (5.88, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.488 (0.644, 3.438)
	Treatment P-value [b]		0.34735
	Interaction P-value [c]		0.71056
Acute kidney injury	No. of Events (%)	3 (7.1)	2 (5.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.431 (0.239, 8.567)
	Treatment P-value [b]		0.69943
	Interaction P-value [c]		0.81987

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Table TEAE.KM.S4.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	21 (50.0)	19 (48.7)
	Median Survival Est. (95% CI)	5.82 (1.87, NC)	5.52 (2.56, NC)
	Hazard Ratio (95% CI) [a]		1.078 (0.580, 2.006)
	Treatment P-value [b]		0.78388
	Interaction P-value [c]		0.23510
Skin and subcutaneous tissue disorders	No. of Events (%)	35 (83.3)	26 (66.7)
	Median Survival Est. (95% CI)	0.56 (0.39, 0.95)	0.76 (0.49, 3.78)
	Hazard Ratio (95% CI) [a]		1.545 (0.930, 2.568)
	Treatment P-value [b]		0.07453
	Interaction P-value [c]		0.33244

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Table TEAE.KM.S4.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Drug eruption	No. of Events (%)	4 (9.5)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.04963
	Interaction P-value [c]		0.94205
Dry skin	No. of Events (%)	13 (31.0)	3 (7.7)
	Median Survival Est. (95% CI)	NC (5.55, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.561 (1.299, 16.014)
	Treatment P-value [b]		0.00896
	Interaction P-value [c]		0.12778

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Subgroup: Region, Level: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Pruritus	No. of Events (%)	20 (47.6)	3 (7.7)
	Median Survival Est. (95% CI)	NC (0.72, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		8.049 (2.391, 27.098)
	Treatment P-value [b]		0.00005
	Interaction P-value [c]		0.24829
Rash	No. of Events (%)	3 (7.1)	4 (10.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.691 (0.155, 3.089)
	Treatment P-value [b]		0.58534
	Interaction P-value [c]		0.02195

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Subgroup: Region, Level: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Rash maculo-papular	No. of Events (%)	20 (47.6)	3 (7.7)
	Median Survival Est. (95% CI)	NC (0.59, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		8.072 (2.396, 27.191)
	Treatment P-value [b]		0.00005
	Interaction P-value [c]		0.98747
Skin hyperpigmentation	No. of Events (%)	6 (14.3)	1 (2.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.979 (0.720, 49.667)
	Treatment P-value [b]		0.05908
	Interaction P-value [c]		0.99993

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Table TEAE.KM.S4.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Any Event	No. of Events (%)	131 (99.2)	128 (99.2)
	Median Survival Est. (95% CI)	0.16 (0.13, 0.23)	0.16 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.996 (0.780, 1.271)
	Treatment P-value [b]		0.93420
	Interaction P-value [c]		0.68127
Blood and lymphatic system disorders	No. of Events (%)	44 (33.3)	49 (38.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (12.94, NC)
	Hazard Ratio (95% CI) [a]		0.818 (0.544, 1.228)
	Treatment P-value [b]		0.31808
	Interaction P-value [c]		0.05004

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Subgroup: Region, Level: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Anaemia	No. of Events (%)	34 (25.8)	31 (24.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.075 (0.661, 1.749)
	Treatment P-value [b]		0.78721
	Interaction P-value [c]		0.00445
Febrile neutropenia	No. of Events (%)	3 (2.3)	10 (7.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.285 (0.078, 1.034)
	Treatment P-value [b]		0.04126
	Interaction P-value [c]		0.99987

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Subgroup: Region, Level: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Eye disorders	No. of Events (%)	22 (16.7)	10 (7.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.231 (1.057, 4.712)
	Treatment P-value [b]		0.02912
	Interaction P-value [c]		0.04826
Lacrimation increased	No. of Events (%)	6 (4.5)	4 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.431 (0.404, 5.072)
	Treatment P-value [b]		0.56570
	Interaction P-value [c]		0.11050

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table TEAE.KM.S4.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Vision blurred	No. of Events (%)	4 (3.0)	3 (2.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.312 (0.294, 5.863)
	Treatment P-value [b]		0.70913
	Interaction P-value [c]		0.34487
Diarrhoea	No. of Events (%)	39 (29.5)	27 (20.9)
	Median Survival Est. (95% CI)	NC (15.11, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.416 (0.867, 2.314)
	Treatment P-value [b]		0.16659
	Interaction P-value [c]		0.02358

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S4.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Dry mouth	No. of Events (%)	7 (5.3)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00828
	Interaction P-value [c]		0.85466
Chills	No. of Events (%)	7 (5.3)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00770
	Interaction P-value [c]		0.41717

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Table TEAE.KM.S4.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Fatigue	No. of Events (%)	46 (34.8)	26 (20.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.790 (1.107, 2.896)
	Treatment P-value [b]		0.01672
	Interaction P-value [c]		0.26690
Infections and infestations	No. of Events (%)	62 (47.0)	39 (30.2)
	Median Survival Est. (95% CI)	10.87 (3.55, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.614 (1.081, 2.410)
	Treatment P-value [b]		0.02263
	Interaction P-value [c]		0.19322

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Table TEAE.KM.S4.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Conjunctivitis	No. of Events (%)	5 (3.8)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.03059
	Interaction P-value [c]		0.32369
Alanine aminotransferase increased	No. of Events (%)	12 (9.1)	1 (0.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		12.352 (1.607, 94.950)
	Treatment P-value [b]		0.00197
	Interaction P-value [c]		0.47337

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Table TEAE.KM.S4.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Aspartate aminotransferase increased	No. of Events (%)	13 (9.8)	2 (1.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.774 (1.529, 30.019)
	Treatment P-value [b]		0.00375
	Interaction P-value [c]		0.68299
Blood creatinine increased	No. of Events (%)	9 (6.8)	2 (1.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.520 (0.977, 20.913)
	Treatment P-value [b]		0.03309
	Interaction P-value [c]		0.82290

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Table TEAE.KM.S4.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Neutrophil count decreased	No. of Events (%)	23 (17.4)	34 (26.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.566 (0.333, 0.961)
	Treatment P-value [b]		0.03983
	Interaction P-value [c]		0.61418
Weight decreased	No. of Events (%)	21 (15.9)	7 (5.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.138 (1.334, 7.383)
	Treatment P-value [b]		0.00604
	Interaction P-value [c]		0.50575

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Subgroup: Region, Level: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
White blood cell count decreased	No. of Events (%)	11 (8.3)	23 (17.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.415 (0.202, 0.852)
	Treatment P-value [b]		0.01539
	Interaction P-value [c]		0.26977
Metabolism and nutrition disorders	No. of Events (%)	81 (61.4)	50 (38.8)
	Median Survival Est. (95% CI)	1.87 (1.05, 5.06)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.844 (1.296, 2.624)
	Treatment P-value [b]		0.00059
	Interaction P-value [c]		0.15788

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Table TEAE.KM.S4.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Decreased appetite	No. of Events (%)	61 (46.2)	31 (24.0)
	Median Survival Est. (95% CI)	NC (4.11, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.131 (1.383, 3.285)
	Treatment P-value [b]		0.00047
	Interaction P-value [c]		0.12069
Hyperglycaemia	No. of Events (%)	9 (6.8)	2 (1.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.553 (0.984, 21.075)
	Treatment P-value [b]		0.03498
	Interaction P-value [c]		0.98065

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Subgroup: Region, Level: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Musculoskeletal and connective tissue disorders	No. of Events (%)	38 (28.8)	45 (34.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.702 (0.456, 1.081)
	Treatment P-value [b]		0.11101
	Interaction P-value [c]		0.55162
Arthralgia	No. of Events (%)	6 (4.5)	14 (10.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.386 (0.148, 1.005)
	Treatment P-value [b]		0.04203
	Interaction P-value [c]		0.41958

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Table TEAE.KM.S4.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Myalgia	No. of Events (%)	3 (2.3)	16 (12.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.171 (0.050, 0.588)
	Treatment P-value [b]		0.00166
	Interaction P-value [c]		0.10858
Nervous system disorders	No. of Events (%)	85 (64.4)	65 (50.4)
	Median Survival Est. (95% CI)	3.09 (2.00, 4.07)	4.53 (2.40, NC)
	Hazard Ratio (95% CI) [a]		1.320 (0.956, 1.824)
	Treatment P-value [b]		0.08390
	Interaction P-value [c]		0.33276

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Subgroup: Region, Level: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Dysgeusia	No. of Events (%)	36 (27.3)	10 (7.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.904 (1.937, 7.867)
	Treatment P-value [b]		0.00004
	Interaction P-value [c]		0.40176
Peripheral sensory neuropathy	No. of Events (%)	50 (37.9)	43 (33.3)
	Median Survival Est. (95% CI)	NC (6.60, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.996 (0.663, 1.498)
	Treatment P-value [b]		0.99676
	Interaction P-value [c]		0.02158

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Subgroup: Region, Level: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Renal and urinary disorders	No. of Events (%)	29 (22.0)	24 (18.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.225 (0.713, 2.104)
	Treatment P-value [b]		0.50334
	Interaction P-value [c]		0.71056
Acute kidney injury	No. of Events (%)	7 (5.3)	3 (2.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.328 (0.602, 9.007)
	Treatment P-value [b]		0.20106
	Interaction P-value [c]		0.81987

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Subgroup: Region, Level: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	44 (33.3)	22 (17.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.083 (1.249, 3.475)
	Treatment P-value [b]		0.00381
	Interaction P-value [c]		0.23510
Skin and subcutaneous tissue disorders	No. of Events (%)	114 (86.4)	76 (58.9)
	Median Survival Est. (95% CI)	0.39 (0.33, 0.49)	0.82 (0.69, 2.37)
	Hazard Ratio (95% CI) [a]		2.331 (1.741, 3.121)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.33244

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Table TEAE.KM.S4.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Drug eruption	No. of Events (%)	18 (13.6)	3 (2.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.164 (1.816, 20.930)
	Treatment P-value [b]		0.00090
	Interaction P-value [c]		0.94205
Dry skin	No. of Events (%)	16 (12.1)	7 (5.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.354 (0.968, 5.723)
	Treatment P-value [b]		0.05427
	Interaction P-value [c]		0.12778

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table TEAE.KM.S4.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Pruritus	No. of Events (%)	54 (40.9)	15 (11.6)
	Median Survival Est. (95% CI)	NC (7.92, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.533 (2.557, 8.036)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.24829
Rash	No. of Events (%)	18 (13.6)	9 (7.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.057 (0.924, 4.580)
	Treatment P-value [b]		0.07052
	Interaction P-value [c]		0.02195

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S4.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Rash maculo-papular	No. of Events (%)	20 (15.2)	3 (2.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.028 (2.088, 23.654)
	Treatment P-value [b]		0.00030
	Interaction P-value [c]		0.98747
Skin hyperpigmentation	No. of Events (%)	11 (8.3)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00072
	Interaction P-value [c]		0.99993

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Table TEAE.KM.S5.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Any Event	No. of Events (%)	117 (97.5)	117 (98.3)
	Median Survival Est. (95% CI)	0.20 (0.13, 0.26)	0.13 (0.10, 0.20)
	Hazard Ratio (95% CI) [a]		1.014 (0.784, 1.311)
	Treatment P-value [b]		0.87629
	Interaction P-value [c]		0.30531
Blood and lymphatic system disorders	No. of Events (%)	27 (22.5)	43 (36.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.553 (0.342, 0.895)
	Treatment P-value [b]		0.01449
	Interaction P-value [c]		0.88622

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table TEAE.KM.S5.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Anaemia	No. of Events (%)	17 (14.2)	33 (27.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.461 (0.257, 0.827)
	Treatment P-value [b]		0.00841
	Interaction P-value [c]		0.22327
Febrile neutropenia	No. of Events (%)	2 (1.7)	3 (2.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.664 (0.111, 3.973)
	Treatment P-value [b]		0.65810
	Interaction P-value [c]		0.19076

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S5.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Eye disorders	No. of Events (%)	31 (25.8)	10 (8.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.483 (1.707, 7.105)
	Treatment P-value [b]		0.00022
	Interaction P-value [c]		0.83848
Dry eye	No. of Events (%)	3 (2.5)	2 (1.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.510 (0.252, 9.035)
	Treatment P-value [b]		0.64252
	Interaction P-value [c]		0.09203

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S5.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Lacrimation increased	No. of Events (%)	11 (9.2)	4 (3.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.871 (0.914, 9.017)
	Treatment P-value [b]		0.05783
	Interaction P-value [c]		0.71431
Vision blurred	No. of Events (%)	6 (5.0)	1 (0.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.167 (0.742, 51.226)
	Treatment P-value [b]		0.05343
	Interaction P-value [c]		0.42692

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S5.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Diarrhoea	No. of Events (%)	41 (34.2)	30 (25.2)
	Median Survival Est. (95% CI)	NC (15.11, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.376 (0.859, 2.204)
	Treatment P-value [b]		0.19013
	Interaction P-value [c]		0.49825
Dry mouth	No. of Events (%)	11 (9.2)	3 (2.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.780 (1.054, 13.550)
	Treatment P-value [b]		0.02921
	Interaction P-value [c]		0.84715

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table TEAE.KM.S5.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Chills	No. of Events (%)	7 (5.8)	1 (0.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.090 (0.872, 57.625)
	Treatment P-value [b]		0.03314
	Interaction P-value [c]		0.28177
Fatigue	No. of Events (%)	37 (30.8)	36 (30.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.979 (0.619, 1.549)
	Treatment P-value [b]		0.91944
	Interaction P-value [c]		0.06118

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table TEAE.KM.S5.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Infections and infestations	No. of Events (%)	60 (50.0)	36 (30.3)
	Median Survival Est. (95% CI)	9.03 (3.84, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.779 (1.176, 2.689)
	Treatment P-value [b]		0.00597
	Interaction P-value [c]		0.33434
Conjunctivitis	No. of Events (%)	10 (8.3)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00134
	Interaction P-value [c]		0.98855

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S5.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Alanine aminotransferase increased	No. of Events (%)	15 (12.5)	1 (0.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		16.121 (2.130, 122.039)
	Treatment P-value [b]		0.00028
	Interaction P-value [c]		0.14575
Aspartate aminotransferase increased	No. of Events (%)	19 (15.8)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.98375

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S5.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Blood creatinine increased	No. of Events (%)	9 (7.5)	1 (0.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.369 (1.188, 73.898)
	Treatment P-value [b]		0.00970
	Interaction P-value [c]		0.28591
Neutrophil count decreased	No. of Events (%)	16 (13.3)	31 (26.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.443 (0.242, 0.810)
	Treatment P-value [b]		0.00798
	Interaction P-value [c]		0.36881

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S5.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Weight decreased	No. of Events (%)	17 (14.2)	8 (6.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.182 (0.942, 5.056)
	Treatment P-value [b]		0.06345
	Interaction P-value [c]		0.74891
White blood cell count decreased	No. of Events (%)	10 (8.3)	17 (14.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.536 (0.245, 1.170)
	Treatment P-value [b]		0.12016
	Interaction P-value [c]		0.53413

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S5.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Metabolism and nutrition disorders	No. of Events (%)	57 (47.5)	44 (37.0)
	Median Survival Est. (95% CI)	NC (2.04, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.359 (0.917, 2.014)
	Treatment P-value [b]		0.13628
	Interaction P-value [c]		0.73842
Decreased appetite	No. of Events (%)	39 (32.5)	29 (24.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.377 (0.851, 2.227)
	Treatment P-value [b]		0.19991
	Interaction P-value [c]		0.53353

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Astellas: 7465-CL-0301
Table TEAE.KM.S5.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Hyperglycaemia	No. of Events (%)	11 (9.2)	2 (1.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.715 (1.267, 25.783)
	Treatment P-value [b]		0.01009
	Interaction P-value [c]		0.88420
Musculoskeletal and connective tissue disorders	No. of Events (%)	38 (31.7)	49 (41.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (5.68, NC)
	Hazard Ratio (95% CI) [a]		0.669 (0.438, 1.022)
	Treatment P-value [b]		0.06220
	Interaction P-value [c]		0.78634

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Table TEAE.KM.S5.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Arthralgia	No. of Events (%)	8 (6.7)	16 (13.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.469 (0.201, 1.097)
	Treatment P-value [b]		0.07547
	Interaction P-value [c]		0.82772
Myalgia	No. of Events (%)	6 (5.0)	11 (9.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.521 (0.193, 1.409)
	Treatment P-value [b]		0.19235
	Interaction P-value [c]		0.65428

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Table TEAE.KM.S5.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Nervous system disorders	No. of Events (%)	85 (70.8)	62 (52.1)
	Median Survival Est. (95% CI)	2.56 (1.54, 3.68)	4.86 (2.14, NC)
	Hazard Ratio (95% CI) [a]		1.524 (1.098, 2.116)
	Treatment P-value [b]		0.01236
	Interaction P-value [c]		0.71859
Dysgeusia	No. of Events (%)	39 (32.5)	12 (10.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.621 (1.896, 6.918)
	Treatment P-value [b]		0.00004
	Interaction P-value [c]		0.82973

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Table TEAE.KM.S5.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Peripheral sensory neuropathy	No. of Events (%)	46 (38.3)	37 (31.1)
	Median Survival Est. (95% CI)	NC (8.34, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.171 (0.759, 1.806)
	Treatment P-value [b]		0.47682
	Interaction P-value [c]		0.16547
Renal and urinary disorders	No. of Events (%)	25 (20.8)	16 (13.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.634 (0.872, 3.061)
	Treatment P-value [b]		0.13100
	Interaction P-value [c]		0.62460

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Table TEAE.KM.S5.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Acute kidney injury	No. of Events (%)	4 (3.3)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.04479
	Interaction P-value [c]		0.98677
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	34 (28.3)	23 (19.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.556 (0.916, 2.641)
	Treatment P-value [b]		0.09731
	Interaction P-value [c]		0.85717

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Table TEAE.KM.S5.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Skin and subcutaneous tissue disorders	No. of Events (%)	103 (85.8)	64 (53.8)
	Median Survival Est. (95% CI)	0.39 (0.33, 0.49)	3.12 (0.72, NC)
	Hazard Ratio (95% CI) [a]		2.606 (1.904, 3.568)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.14032
Drug eruption	No. of Events (%)	18 (15.0)	3 (2.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.418 (1.890, 21.792)
	Treatment P-value [b]		0.00073
	Interaction P-value [c]		0.88230

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Subgroup: ECOG PS from IRT Strata, Level: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Dry skin	No. of Events (%)	18 (15.0)	5 (4.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.845 (1.427, 10.357)
	Treatment P-value [b]		0.00407
	Interaction P-value [c]		0.61182
Pruritus	No. of Events (%)	49 (40.8)	11 (9.2)
	Median Survival Est. (95% CI)	NC (5.55, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.544 (2.881, 10.665)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.69747

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Subgroup: ECOG PS from IRT Strata, Level: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Rash	No. of Events (%)	20 (16.7)	7 (5.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.044 (1.287, 7.200)
	Treatment P-value [b]		0.00806
	Interaction P-value [c]		0.99579
Rash maculo-papular	No. of Events (%)	24 (20.0)	2 (1.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		13.395 (3.166, 56.683)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.43192

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Subgroup: ECOG PS from IRT Strata, Level: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Skin hyperpigmentation	No. of Events (%)	13 (10.8)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00022
	Interaction P-value [c]		0.99173

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Table TEAE.KM.S5.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Any Event	No. of Events (%)	173 (98.3)	171 (99.4)
	Median Survival Est. (95% CI)	0.20 (0.16, 0.23)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.852 (0.689, 1.053)
	Treatment P-value [b]		0.13195
	Interaction P-value [c]		0.30531
Blood and lymphatic system disorders	No. of Events (%)	58 (33.0)	80 (46.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	7.26 (2.33, NC)
	Hazard Ratio (95% CI) [a]		0.577 (0.412, 0.810)
	Treatment P-value [b]		0.00143
	Interaction P-value [c]		0.88622

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Subgroup: ECOG PS from IRT Strata, Level: 1

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Anaemia	No. of Events (%)	43 (24.4)	54 (31.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.716 (0.479, 1.069)
	Treatment P-value [b]		0.09874
	Interaction P-value [c]		0.22327
Febrile neutropenia	No. of Events (%)	2 (1.1)	13 (7.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.140 (0.032, 0.622)
	Treatment P-value [b]		0.00288
	Interaction P-value [c]		0.19076

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Subgroup: ECOG PS from IRT Strata, Level: 1

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Eye disorders	No. of Events (%)	49 (27.8)	16 (9.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.169 (1.802, 5.572)
	Treatment P-value [b]		0.00002
	Interaction P-value [c]		0.83848
Dry eye	No. of Events (%)	16 (9.1)	1 (0.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		15.360 (2.036, 115.862)
	Treatment P-value [b]		0.00040
	Interaction P-value [c]		0.09203

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Subgroup: ECOG PS from IRT Strata, Level: 1

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Lacrimation increased	No. of Events (%)	19 (10.8)	8 (4.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.206 (0.965, 5.040)
	Treatment P-value [b]		0.05115
	Interaction P-value [c]		0.71431
Vision blurred	No. of Events (%)	10 (5.7)	4 (2.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.318 (0.727, 7.393)
	Treatment P-value [b]		0.14821
	Interaction P-value [c]		0.42692

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Subgroup: ECOG PS from IRT Strata, Level: 1

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Diarrhoea	No. of Events (%)	62 (35.2)	37 (21.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.706 (1.135, 2.564)
	Treatment P-value [b]		0.00916
	Interaction P-value [c]		0.49825
Dry mouth	No. of Events (%)	13 (7.4)	4 (2.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.198 (1.043, 9.810)
	Treatment P-value [b]		0.03122
	Interaction P-value [c]		0.84715

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Astellas: 7465-CL-0301
Table TEAE.KM.S5.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Chills	No. of Events (%)	10 (5.7)	5 (2.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.946 (0.665, 5.695)
	Treatment P-value [b]		0.22702
	Interaction P-value [c]		0.28177
Fatigue	No. of Events (%)	71 (40.3)	42 (24.4)
	Median Survival Est. (95% CI)	NC (6.14, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.731 (1.182, 2.535)
	Treatment P-value [b]		0.00448
	Interaction P-value [c]		0.06118

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Subgroup: ECOG PS from IRT Strata, Level: 1

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Infections and infestations	No. of Events (%)	92 (52.3)	69 (40.1)
	Median Survival Est. (95% CI)	3.94 (2.73, NC)	NC (5.52, NC)
	Hazard Ratio (95% CI) [a]		1.378 (1.008, 1.883)
	Treatment P-value [b]		0.04385
	Interaction P-value [c]		0.33434
Conjunctivitis	No. of Events (%)	9 (5.1)	2 (1.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.259 (0.920, 19.719)
	Treatment P-value [b]		0.04378
	Interaction P-value [c]		0.98855

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Subgroup: ECOG PS from IRT Strata, Level: 1

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Alanine aminotransferase increased	No. of Events (%)	12 (6.8)	4 (2.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.883 (0.930, 8.940)
	Treatment P-value [b]		0.05452
	Interaction P-value [c]		0.14575
Aspartate aminotransferase increased	No. of Events (%)	17 (9.7)	5 (2.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.266 (1.205, 8.854)
	Treatment P-value [b]		0.01412
	Interaction P-value [c]		0.98375

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Subgroup: ECOG PS from IRT Strata, Level: 1

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Blood creatinine increased	No. of Events (%)	17 (9.7)	6 (3.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.729 (1.076, 6.924)
	Treatment P-value [b]		0.02714
	Interaction P-value [c]		0.28591
Neutrophil count decreased	No. of Events (%)	17 (9.7)	23 (13.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.660 (0.353, 1.236)
	Treatment P-value [b]		0.17037
	Interaction P-value [c]		0.36881

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Subgroup: ECOG PS from IRT Strata, Level: 1

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Weight decreased	No. of Events (%)	31 (17.6)	12 (7.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.600 (1.335, 5.062)
	Treatment P-value [b]		0.00361
	Interaction P-value [c]		0.74891
White blood cell count decreased	No. of Events (%)	6 (3.4)	15 (8.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.363 (0.141, 0.936)
	Treatment P-value [b]		0.02715
	Interaction P-value [c]		0.53413

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Subgroup: ECOG PS from IRT Strata, Level: 1

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Metabolism and nutrition disorders	No. of Events (%)	117 (66.5)	82 (47.7)
	Median Survival Est. (95% CI)	1.71 (1.02, 2.89)	5.68 (2.60, NC)
	Hazard Ratio (95% CI) [a]		1.476 (1.113, 1.957)
	Treatment P-value [b]		0.00602
	Interaction P-value [c]		0.73842
Decreased appetite	No. of Events (%)	82 (46.6)	49 (28.5)
	Median Survival Est. (95% CI)	9.10 (4.11, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.665 (1.168, 2.372)
	Treatment P-value [b]		0.00439
	Interaction P-value [c]		0.53353

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Subgroup: ECOG PS from IRT Strata, Level: 1

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Hyperglycaemia	No. of Events (%)	20 (11.4)	4 (2.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.981 (1.702, 14.573)
	Treatment P-value [b]		0.00114
	Interaction P-value [c]		0.88420
Musculoskeletal and connective tissue disorders	No. of Events (%)	62 (35.2)	71 (41.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (4.67, NC)
	Hazard Ratio (95% CI) [a]		0.721 (0.513, 1.014)
	Treatment P-value [b]		0.06051
	Interaction P-value [c]		0.78634

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Subgroup: ECOG PS from IRT Strata, Level: 1

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Arthralgia	No. of Events (%)	12 (6.8)	20 (11.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.531 (0.259, 1.086)
	Treatment P-value [b]		0.07185
	Interaction P-value [c]		0.82772
Myalgia	No. of Events (%)	9 (5.1)	21 (12.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.390 (0.179, 0.852)
	Treatment P-value [b]		0.01472
	Interaction P-value [c]		0.65428

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Subgroup: ECOG PS from IRT Strata, Level: 1

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Nervous system disorders	No. of Events (%)	104 (59.1)	75 (43.6)
	Median Survival Est. (95% CI)	2.96 (2.46, 4.14)	7.66 (3.98, NC)
	Hazard Ratio (95% CI) [a]		1.405 (1.044, 1.891)
	Treatment P-value [b]		0.02203
	Interaction P-value [c]		0.71859
Dysgeusia	No. of Events (%)	35 (19.9)	11 (6.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.268 (1.659, 6.434)
	Treatment P-value [b]		0.00027
	Interaction P-value [c]		0.82973

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Subgroup: ECOG PS from IRT Strata, Level: 1

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Peripheral sensory neuropathy	No. of Events (%)	56 (31.8)	29 (16.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.820 (1.163, 2.850)
	Treatment P-value [b]		0.00783
	Interaction P-value [c]		0.16547
Renal and urinary disorders	No. of Events (%)	50 (28.4)	36 (20.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.352 (0.881, 2.075)
	Treatment P-value [b]		0.16409
	Interaction P-value [c]		0.62460

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Subgroup: ECOG PS from IRT Strata, Level: 1

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Acute kidney injury	No. of Events (%)	15 (8.5)	8 (4.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.809 (0.767, 4.267)
	Treatment P-value [b]		0.16885
	Interaction P-value [c]		0.98677
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	67 (38.1)	45 (26.2)
	Median Survival Est. (95% CI)	NC (6.64, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.465 (1.004, 2.138)
	Treatment P-value [b]		0.04669
	Interaction P-value [c]		0.85717

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Subgroup: ECOG PS from IRT Strata, Level: 1

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Skin and subcutaneous tissue disorders	No. of Events (%)	134 (76.1)	86 (50.0)
	Median Survival Est. (95% CI)	0.89 (0.66, 0.99)	3.02 (1.41, NC)
	Hazard Ratio (95% CI) [a]		1.909 (1.455, 2.505)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.14032
Drug eruption	No. of Events (%)	8 (4.5)	1 (0.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.701 (0.963, 61.577)
	Treatment P-value [b]		0.02506
	Interaction P-value [c]		0.88230

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System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Dry skin	No. of Events (%)	32 (18.2)	6 (3.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.412 (2.263, 12.943)
	Treatment P-value [b]		0.00002
	Interaction P-value [c]		0.61182
Pruritus	No. of Events (%)	53 (30.1)	9 (5.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.710 (3.310, 13.605)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.69747

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Astellas: 7465-CL-0301
Table TEAE.KM.S5.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Rash	No. of Events (%)	30 (17.0)	10 (5.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.035 (1.483, 6.210)
	Treatment P-value [b]		0.00133
	Interaction P-value [c]		0.99579
Rash maculo-papular	No. of Events (%)	26 (14.8)	4 (2.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.546 (2.284, 18.757)
	Treatment P-value [b]		0.00005
	Interaction P-value [c]		0.43192

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table TEAE.KM.S5.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Skin hyperpigmentation	No. of Events (%)	6 (3.4)	1 (0.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.925 (0.713, 49.220)
	Treatment P-value [b]		0.05873
	Interaction P-value [c]		0.99173

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Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table TEAE.KM.S6.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Any Event	No. of Events (%)	90 (97.8)	84 (96.6)
	Median Survival Est. (95% CI)	0.16 (0.13, 0.23)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		1.087 (0.806, 1.465)
	Treatment P-value [b]		0.74580
	Interaction P-value [c]		0.17954
Blood and lymphatic system disorders	No. of Events (%)	30 (32.6)	36 (41.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (2.14, NC)
	Hazard Ratio (95% CI) [a]		0.704 (0.433, 1.142)
	Treatment P-value [b]		0.15988
	Interaction P-value [c]		0.33065

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Table TEAE.KM.S6.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Anaemia	No. of Events (%)	20 (21.7)	23 (26.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.805 (0.442, 1.466)
	Treatment P-value [b]		0.51151
	Interaction P-value [c]		0.30817
Febrile neutropenia	No. of Events (%)	2 (2.2)	6 (6.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.305 (0.062, 1.514)
	Treatment P-value [b]		0.13327
	Interaction P-value [c]		0.68061

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Table TEAE.KM.S6.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Eye disorders	No. of Events (%)	20 (21.7)	7 (8.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.912 (1.231, 6.888)
	Treatment P-value [b]		0.01003
	Interaction P-value [c]		0.73707
Dry eye	No. of Events (%)	6 (6.5)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.01686
	Interaction P-value [c]		0.99041

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Table TEAE.KM.S6.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Lacrimation increased	No. of Events (%)	7 (7.6)	2 (2.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.200 (0.665, 15.405)
	Treatment P-value [b]		0.12449
	Interaction P-value [c]		0.71429
Vision blurred	No. of Events (%)	7 (7.6)	3 (3.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.157 (0.557, 8.345)
	Treatment P-value [b]		0.25657
	Interaction P-value [c]		0.48810

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Table TEAE.KM.S6.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Diarrhoea	No. of Events (%)	27 (29.3)	17 (19.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.570 (0.856, 2.881)
	Treatment P-value [b]		0.13216
	Interaction P-value [c]		0.98001
Dry mouth	No. of Events (%)	7 (7.6)	4 (4.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.711 (0.501, 5.848)
	Treatment P-value [b]		0.39359
	Interaction P-value [c]		0.17166

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Table TEAE.KM.S6.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Chills	No. of Events (%)	5 (5.4)	3 (3.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.581 (0.378, 6.618)
	Treatment P-value [b]		0.49822
	Interaction P-value [c]		0.33739
Fatigue	No. of Events (%)	32 (34.8)	24 (27.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.269 (0.748, 2.155)
	Treatment P-value [b]		0.35598
	Interaction P-value [c]		0.72609

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Table TEAE.KM.S6.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Infections and infestations	No. of Events (%)	46 (50.0)	30 (34.5)
	Median Survival Est. (95% CI)	8.64 (2.37, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.510 (0.953, 2.393)
	Treatment P-value [b]		0.08651
	Interaction P-value [c]		0.98414
Conjunctivitis	No. of Events (%)	10 (10.9)	1 (1.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.387 (1.201, 73.375)
	Treatment P-value [b]		0.01106
	Interaction P-value [c]		0.97821

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S6.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Alanine aminotransferase increased	No. of Events (%)	7 (7.6)	2 (2.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.306 (0.687, 15.916)
	Treatment P-value [b]		0.11544
	Interaction P-value [c]		0.46769
Amylase increased	No. of Events (%)	1 (1.1)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.36131
	Interaction P-value [c]		0.99374

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Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Aspartate aminotransferase increased	No. of Events (%)	9 (9.8)	2 (2.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.264 (0.921, 19.738)
	Treatment P-value [b]		0.04628
	Interaction P-value [c]		0.42121
Blood creatinine increased	No. of Events (%)	7 (7.6)	2 (2.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.334 (0.692, 16.052)
	Treatment P-value [b]		0.10743
	Interaction P-value [c]		0.87752

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Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Neutrophil count decreased	No. of Events (%)	13 (14.1)	12 (13.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.944 (0.430, 2.069)
	Treatment P-value [b]		0.88253
	Interaction P-value [c]		0.09430
Weight decreased	No. of Events (%)	12 (13.0)	9 (10.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.251 (0.527, 2.969)
	Treatment P-value [b]		0.60578
	Interaction P-value [c]		0.07160

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
White blood cell count decreased	No. of Events (%)	2 (2.2)	4 (4.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.454 (0.083, 2.481)
	Treatment P-value [b]		0.38082
	Interaction P-value [c]		0.99918
Metabolism and nutrition disorders	No. of Events (%)	55 (59.8)	37 (42.5)
	Median Survival Est. (95% CI)	1.38 (0.72, 4.90)	NC (2.46, NC)
	Hazard Ratio (95% CI) [a]		1.584 (1.044, 2.404)
	Treatment P-value [b]		0.03144
	Interaction P-value [c]		0.58405

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S6.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Decreased appetite	No. of Events (%)	39 (42.4)	25 (28.7)
	Median Survival Est. (95% CI)	NC (2.79, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.539 (0.931, 2.543)
	Treatment P-value [b]		0.09160
	Interaction P-value [c]		0.94739
Hyperglycaemia	No. of Events (%)	10 (10.9)	1 (1.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		10.010 (1.281, 78.198)
	Treatment P-value [b]		0.00684
	Interaction P-value [c]		0.46440

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Astellas: 7465-CL-0301
Table TEAE.KM.S6.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Musculoskeletal and connective tissue disorders	No. of Events (%)	26 (28.3)	36 (41.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (2.30, NC)
	Hazard Ratio (95% CI) [a]		0.578 (0.349, 0.957)
	Treatment P-value [b]		0.02905
	Interaction P-value [c]		0.37015
Arthralgia	No. of Events (%)	7 (7.6)	8 (9.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.776 (0.281, 2.141)
	Treatment P-value [b]		0.57480
	Interaction P-value [c]		0.32931

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table TEAE.KM.S6.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Myalgia	No. of Events (%)	2 (2.2)	10 (11.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.180 (0.039, 0.822)
	Treatment P-value [b]		0.01278
	Interaction P-value [c]		0.18388
Nervous system disorders	No. of Events (%)	48 (52.2)	41 (47.1)
	Median Survival Est. (95% CI)	4.04 (2.20, NC)	5.49 (2.43, NC)
	Hazard Ratio (95% CI) [a]		1.091 (0.719, 1.656)
	Treatment P-value [b]		0.64486
	Interaction P-value [c]		0.10877

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Table TEAE.KM.S6.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Dysgeusia	No. of Events (%)	15 (16.3)	8 (9.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.797 (0.762, 4.240)
	Treatment P-value [b]		0.17245
	Interaction P-value [c]		0.09109
Peripheral sensory neuropathy	No. of Events (%)	24 (26.1)	15 (17.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.402 (0.735, 2.672)
	Treatment P-value [b]		0.30225
	Interaction P-value [c]		0.87699

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Table TEAE.KM.S6.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Renal and urinary disorders	No. of Events (%)	19 (20.7)	13 (14.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.404 (0.694, 2.843)
	Treatment P-value [b]		0.32356
	Interaction P-value [c]		0.91346
Acute kidney injury	No. of Events (%)	5 (5.4)	3 (3.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.587 (0.379, 6.642)
	Treatment P-value [b]		0.58241
	Interaction P-value [c]		0.53192

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Table TEAE.KM.S6.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	32 (34.8)	20 (23.0)
	Median Survival Est. (95% CI)	NC (5.13, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.613 (0.923, 2.820)
	Treatment P-value [b]		0.09077
	Interaction P-value [c]		0.77226
Skin and subcutaneous tissue disorders	No. of Events (%)	66 (71.7)	45 (51.7)
	Median Survival Est. (95% CI)	0.62 (0.39, 0.95)	2.37 (1.12, NC)
	Hazard Ratio (95% CI) [a]		1.930 (1.321, 2.822)
	Treatment P-value [b]		0.00059
	Interaction P-value [c]		0.50244

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Table TEAE.KM.S6.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Drug eruption	No. of Events (%)	8 (8.7)	2 (2.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.843 (0.816, 18.105)
	Treatment P-value [b]		0.06107
	Interaction P-value [c]		0.42139
Dry skin	No. of Events (%)	15 (16.3)	5 (5.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.952 (1.073, 8.125)
	Treatment P-value [b]		0.02555
	Interaction P-value [c]		0.27720

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Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Pruritus	No. of Events (%)	32 (34.8)	6 (6.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.211 (2.596, 14.859)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.93372
Rash	No. of Events (%)	10 (10.9)	5 (5.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.859 (0.635, 5.440)
	Treatment P-value [b]		0.25241
	Interaction P-value [c]		0.30028

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Table TEAE.KM.S6.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Rash erythematous	No. of Events (%)	1 (1.1)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.35734
	Interaction P-value [c]		0.99462
Rash maculo-papular	No. of Events (%)	18 (19.6)	2 (2.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.498 (2.203, 40.948)
	Treatment P-value [b]		0.00021
	Interaction P-value [c]		0.89327

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Table TEAE.KM.S6.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Skin hyperpigmentation	No. of Events (%)	3 (3.3)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.08265
	Interaction P-value [c]		0.99267

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Table TEAE.KM.S6.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Any Event	No. of Events (%)	200 (98.0)	204 (100.0)
	Median Survival Est. (95% CI)	0.21 (0.16, 0.26)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.851 (0.700, 1.035)
	Treatment P-value [b]		0.11262
	Interaction P-value [c]		0.17954
Blood and lymphatic system disorders	No. of Events (%)	55 (27.0)	87 (42.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (5.68, NC)
	Hazard Ratio (95% CI) [a]		0.525 (0.374, 0.736)
	Treatment P-value [b]		0.00013
	Interaction P-value [c]		0.33065

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Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Anaemia	No. of Events (%)	40 (19.6)	64 (31.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.554 (0.373, 0.823)
	Treatment P-value [b]		0.00269
	Interaction P-value [c]		0.30817
Febrile neutropenia	No. of Events (%)	2 (1.0)	10 (4.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.192 (0.042, 0.877)
	Treatment P-value [b]		0.01712
	Interaction P-value [c]		0.68061

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Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Eye disorders	No. of Events (%)	60 (29.4)	19 (9.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.458 (2.064, 5.794)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.73707
Dry eye	No. of Events (%)	13 (6.4)	3 (1.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.317 (1.230, 15.150)
	Treatment P-value [b]		0.01272
	Interaction P-value [c]		0.99041

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Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Lacrimation increased	No. of Events (%)	23 (11.3)	10 (4.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.313 (1.101, 4.860)
	Treatment P-value [b]		0.02275
	Interaction P-value [c]		0.71429
Vision blurred	No. of Events (%)	9 (4.4)	2 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.445 (0.960, 20.569)
	Treatment P-value [b]		0.03636
	Interaction P-value [c]		0.48810

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Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Diarrhoea	No. of Events (%)	76 (37.3)	50 (24.5)
	Median Survival Est. (95% CI)	NC (15.11, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.556 (1.089, 2.224)
	Treatment P-value [b]		0.01391
	Interaction P-value [c]		0.98001
Dry mouth	No. of Events (%)	17 (8.3)	3 (1.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.746 (1.684, 19.608)
	Treatment P-value [b]		0.00158
	Interaction P-value [c]		0.17166

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Astellas: 7465-CL-0301
Table TEAE.KM.S6.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Chills	No. of Events (%)	12 (5.9)	3 (1.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.027 (1.137, 14.271)
	Treatment P-value [b]		0.01963
	Interaction P-value [c]		0.33739
Fatigue	No. of Events (%)	76 (37.3)	54 (26.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.422 (1.003, 2.015)
	Treatment P-value [b]		0.04578
	Interaction P-value [c]		0.72609

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Table TEAE.KM.S6.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Infections and infestations	No. of Events (%)	106 (52.0)	75 (36.8)
	Median Survival Est. (95% CI)	5.45 (3.45, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.519 (1.130, 2.042)
	Treatment P-value [b]		0.00497
	Interaction P-value [c]		0.98414
Conjunctivitis	No. of Events (%)	9 (4.4)	1 (0.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.013 (1.142, 71.144)
	Treatment P-value [b]		0.01131
	Interaction P-value [c]		0.97821

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Table TEAE.KM.S6.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Alanine aminotransferase increased	No. of Events (%)	20 (9.8)	3 (1.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.900 (2.050, 23.219)
	Treatment P-value [b]		0.00030
	Interaction P-value [c]		0.46769
Amylase increased	No. of Events (%)	10 (4.9)	2 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.948 (1.084, 22.584)
	Treatment P-value [b]		0.02194
	Interaction P-value [c]		0.99374

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S6.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Aspartate aminotransferase increased	No. of Events (%)	27 (13.2)	3 (1.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.460 (2.870, 31.185)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.42121
Blood creatinine increased	No. of Events (%)	19 (9.3)	5 (2.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.857 (1.440, 10.330)
	Treatment P-value [b]		0.00386
	Interaction P-value [c]		0.87752

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Table TEAE.KM.S6.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Neutrophil count decreased	No. of Events (%)	20 (9.8)	42 (20.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.420 (0.247, 0.715)
	Treatment P-value [b]		0.00109
	Interaction P-value [c]		0.09430
Weight decreased	No. of Events (%)	36 (17.6)	11 (5.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.428 (1.745, 6.735)
	Treatment P-value [b]		0.00014
	Interaction P-value [c]		0.07160

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S6.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
White blood cell count decreased	No. of Events (%)	14 (6.9)	28 (13.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.455 (0.239, 0.864)
	Treatment P-value [b]		0.01430
	Interaction P-value [c]		0.99918
Metabolism and nutrition disorders	No. of Events (%)	119 (58.3)	89 (43.6)
	Median Survival Est. (95% CI)	3.06 (1.84, 5.78)	NC (5.68, NC)
	Hazard Ratio (95% CI) [a]		1.378 (1.047, 1.814)
	Treatment P-value [b]		0.01889
	Interaction P-value [c]		0.58405

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Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Decreased appetite	No. of Events (%)	82 (40.2)	53 (26.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.571 (1.112, 2.219)
	Treatment P-value [b]		0.00939
	Interaction P-value [c]		0.94739
Hyperglycaemia	No. of Events (%)	21 (10.3)	5 (2.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.282 (1.614, 11.355)
	Treatment P-value [b]		0.00143
	Interaction P-value [c]		0.46440

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Table TEAE.KM.S6.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Musculoskeletal and connective tissue disorders	No. of Events (%)	74 (36.3)	84 (41.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (7.59, NC)
	Hazard Ratio (95% CI) [a]		0.758 (0.554, 1.036)
	Treatment P-value [b]		0.08736
	Interaction P-value [c]		0.37015
Arthralgia	No. of Events (%)	13 (6.4)	28 (13.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.425 (0.220, 0.821)
	Treatment P-value [b]		0.00948
	Interaction P-value [c]		0.32931

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Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Myalgia	No. of Events (%)	13 (6.4)	22 (10.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.557 (0.281, 1.106)
	Treatment P-value [b]		0.09154
	Interaction P-value [c]		0.18388
Nervous system disorders	No. of Events (%)	141 (69.1)	96 (47.1)
	Median Survival Est. (95% CI)	2.69 (1.87, 3.09)	7.66 (3.94, NC)
	Hazard Ratio (95% CI) [a]		1.632 (1.258, 2.116)
	Treatment P-value [b]		0.00018
	Interaction P-value [c]		0.10877

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Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Dysgeusia	No. of Events (%)	59 (28.9)	15 (7.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.363 (2.475, 7.691)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.09109
Peripheral sensory neuropathy	No. of Events (%)	78 (38.2)	51 (25.0)
	Median Survival Est. (95% CI)	NC (8.61, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.485 (1.044, 2.115)
	Treatment P-value [b]		0.02665
	Interaction P-value [c]		0.87699

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Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Renal and urinary disorders	No. of Events (%)	56 (27.5)	39 (19.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.469 (0.976, 2.211)
	Treatment P-value [b]		0.06624
	Interaction P-value [c]		0.91346
Acute kidney injury	No. of Events (%)	14 (6.9)	5 (2.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.780 (1.001, 7.718)
	Treatment P-value [b]		0.03886
	Interaction P-value [c]		0.53192

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Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	69 (33.8)	48 (23.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.461 (1.011, 2.112)
	Treatment P-value [b]		0.04115
	Interaction P-value [c]		0.77226
Skin and subcutaneous tissue disorders	No. of Events (%)	171 (83.8)	105 (51.5)
	Median Survival Est. (95% CI)	0.66 (0.46, 0.82)	3.42 (0.82, NC)
	Hazard Ratio (95% CI) [a]		2.252 (1.763, 2.876)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.50244

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Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Drug eruption	No. of Events (%)	18 (8.8)	2 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.208 (2.136, 39.682)
	Treatment P-value [b]		0.00030
	Interaction P-value [c]		0.42139
Dry skin	No. of Events (%)	35 (17.2)	6 (2.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.180 (2.599, 14.693)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.27720

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[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table TEAE.KM.S6.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Pruritus	No. of Events (%)	70 (34.3)	14 (6.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.942 (3.347, 10.550)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.93372
Rash	No. of Events (%)	40 (19.6)	12 (5.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.604 (1.891, 6.871)
	Treatment P-value [b]		0.00003
	Interaction P-value [c]		0.30028

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Table TEAE.KM.S6.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Rash erythematous	No. of Events (%)	9 (4.4)	1 (0.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.079 (1.150, 71.659)
	Treatment P-value [b]		0.01090
	Interaction P-value [c]		0.99462
Rash maculo-papular	No. of Events (%)	32 (15.7)	4 (2.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		8.401 (2.971, 23.755)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.89327

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S6.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Skin hyperpigmentation	No. of Events (%)	16 (7.8)	1 (0.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		16.462 (2.183, 124.132)
	Treatment P-value [b]		0.00022
	Interaction P-value [c]		0.99267

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Astellas: 7465-CL-0301
Table TEAE.KM.S7.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Any Event	No. of Events (%)	137 (97.9)	106 (99.1)
	Median Survival Est. (95% CI)	0.16 (0.13, 0.23)	0.16 (0.10, 0.26)
	Hazard Ratio (95% CI) [a]		1.179 (0.913, 1.521)
	Treatment P-value [b]		0.22166
	Interaction P-value [c]		0.03090
Blood and lymphatic system disorders	No. of Events (%)	43 (30.7)	29 (27.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.134 (0.708, 1.816)
	Treatment P-value [b]		0.63383
	Interaction P-value [c]		0.00244

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Astellas: 7465-CL-0301
Table TEAE.KM.S7.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Anaemia	No. of Events (%)	35 (25.0)	19 (17.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.426 (0.816, 2.493)
	Treatment P-value [b]		0.21505
	Interaction P-value [c]		0.00105
Eye disorders	No. of Events (%)	35 (25.0)	8 (7.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.684 (1.709, 7.942)
	Treatment P-value [b]		0.00035
	Interaction P-value [c]		0.05831

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S7.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Dry eye	No. of Events (%)	11 (7.9)	1 (0.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		8.385 (1.082, 64.951)
	Treatment P-value [b]		0.01385
	Interaction P-value [c]		0.76374
Lacrimation increased	No. of Events (%)	15 (10.7)	1 (0.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		11.562 (1.529, 87.430)
	Treatment P-value [b]		0.00249
	Interaction P-value [c]		0.01021

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Table TEAE.KM.S7.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Diarrhoea	No. of Events (%)	48 (34.3)	18 (16.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.230 (1.297, 3.835)
	Treatment P-value [b]		0.00265
	Interaction P-value [c]		0.00461
Dry mouth	No. of Events (%)	13 (9.3)	1 (0.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		10.189 (1.333, 77.888)
	Treatment P-value [b]		0.00555
	Interaction P-value [c]		0.13877

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S7.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Chills	No. of Events (%)	9 (6.4)	3 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.304 (0.624, 8.513)
	Treatment P-value [b]		0.19647
	Interaction P-value [c]		0.94074
Fatigue	No. of Events (%)	56 (40.0)	36 (33.6)
	Median Survival Est. (95% CI)	NC (6.51, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.237 (0.814, 1.880)
	Treatment P-value [b]		0.30685
	Interaction P-value [c]		0.33056

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table TEAE.KM.S7.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Infections and infestations	No. of Events (%)	69 (49.3)	42 (39.3)
	Median Survival Est. (95% CI)	9.03 (3.52, NC)	NC (6.21, NC)
	Hazard Ratio (95% CI) [a]		1.301 (0.886, 1.909)
	Treatment P-value [b]		0.17748
	Interaction P-value [c]		0.59213
Conjunctivitis	No. of Events (%)	3 (2.1)	1 (0.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.227 (0.232, 21.411)
	Treatment P-value [b]		0.50484
	Interaction P-value [c]		0.53991

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The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Alanine aminotransferase increased	No. of Events (%)	13 (9.3)	1 (0.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		10.116 (1.324, 77.324)
	Treatment P-value [b]		0.00564
	Interaction P-value [c]		0.69145
Aspartate aminotransferase increased	No. of Events (%)	18 (12.9)	1 (0.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		14.367 (1.919, 107.567)
	Treatment P-value [b]		0.00059
	Interaction P-value [c]		0.66797

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Blood creatinine increased	No. of Events (%)	10 (7.1)	3 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.556 (0.703, 9.288)
	Treatment P-value [b]		0.13243
	Interaction P-value [c]		0.54218
Neutrophil count decreased	No. of Events (%)	16 (11.4)	13 (12.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.896 (0.431, 1.862)
	Treatment P-value [b]		0.74521
	Interaction P-value [c]		0.27741

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S7.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Weight decreased	No. of Events (%)	24 (17.1)	7 (6.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.715 (1.170, 6.302)
	Treatment P-value [b]		0.01586
	Interaction P-value [c]		0.04747
White blood cell count decreased	No. of Events (%)	5 (3.6)	7 (6.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.526 (0.167, 1.657)
	Treatment P-value [b]		0.26725
	Interaction P-value [c]		0.94017

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Metabolism and nutrition disorders	No. of Events (%)	87 (62.1)	31 (29.0)
	Median Survival Est. (95% CI)	2.20 (1.41, 3.94)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.676 (1.775, 4.034)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.00030
Decreased appetite	No. of Events (%)	61 (43.6)	16 (15.0)
	Median Survival Est. (95% CI)	NC (4.90, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.297 (1.901, 5.719)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.00209

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Hyperglycaemia	No. of Events (%)	12 (8.6)	2 (1.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.684 (1.048, 20.929)
	Treatment P-value [b]		0.02626
	Interaction P-value [c]		0.79581
Musculoskeletal and connective tissue disorders	No. of Events (%)	53 (37.9)	52 (48.6)
	Median Survival Est. (95% CI)	NC (7.59, NC)	5.68 (1.35, NC)
	Hazard Ratio (95% CI) [a]		0.599 (0.409, 0.879)
	Treatment P-value [b]		0.00925
	Interaction P-value [c]		0.68375

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table TEAE.KM.S7.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Arthralgia	No. of Events (%)	10 (7.1)	21 (19.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.311 (0.146, 0.661)
	Treatment P-value [b]		0.00143
	Interaction P-value [c]		0.28933
Myalgia	No. of Events (%)	9 (6.4)	17 (15.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.375 (0.167, 0.841)
	Treatment P-value [b]		0.01419
	Interaction P-value [c]		0.97017

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table TEAE.KM.S7.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Nervous system disorders	No. of Events (%)	87 (62.1)	67 (62.6)
	Median Survival Est. (95% CI)	3.25 (2.46, 4.14)	2.40 (1.15, 3.68)
	Hazard Ratio (95% CI) [a]		0.831 (0.604, 1.142)
	Treatment P-value [b]		0.24813
	Interaction P-value [c]		0.00007
Dysgeusia	No. of Events (%)	31 (22.1)	3 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		8.550 (2.614, 27.966)
	Treatment P-value [b]		0.00002
	Interaction P-value [c]		0.23547

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S7.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Peripheral sensory neuropathy	No. of Events (%)	55 (39.3)	41 (38.3)
	Median Survival Est. (95% CI)	NC (5.72, NC)	NC (6.74, NC)
	Hazard Ratio (95% CI) [a]		0.812 (0.542, 1.218)
	Treatment P-value [b]		0.31487
	Interaction P-value [c]		0.00202
Renal and urinary disorders	No. of Events (%)	40 (28.6)	16 (15.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.036 (1.140, 3.635)
	Treatment P-value [b]		0.01351
	Interaction P-value [c]		0.28941

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S7.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Acute kidney injury	No. of Events (%)	11 (7.9)	2 (1.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.210 (0.933, 18.993)
	Treatment P-value [b]		0.04049
	Interaction P-value [c]		0.37645
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	48 (34.3)	32 (29.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.143 (0.731, 1.788)
	Treatment P-value [b]		0.55858
	Interaction P-value [c]		0.27993

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S7.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Skin and subcutaneous tissue disorders	No. of Events (%)	113 (80.7)	71 (66.4)
	Median Survival Est. (95% CI)	0.54 (0.39, 0.82)	0.69 (0.59, 0.95)
	Hazard Ratio (95% CI) [a]		1.426 (1.059, 1.919)
	Treatment P-value [b]		0.02176
	Interaction P-value [c]		0.00213
Drug eruption	No. of Events (%)	17 (12.1)	3 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.379 (1.283, 14.942)
	Treatment P-value [b]		0.00993
	Interaction P-value [c]		0.89193

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Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Dry skin	No. of Events (%)	21 (15.0)	6 (5.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.737 (1.105, 6.781)
	Treatment P-value [b]		0.02455
	Interaction P-value [c]		0.29510
Pruritus	No. of Events (%)	53 (37.9)	11 (10.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.430 (2.314, 8.483)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.31160

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Rash	No. of Events (%)	17 (12.1)	7 (6.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.871 (0.776, 4.511)
	Treatment P-value [b]		0.15544
	Interaction P-value [c]		0.15527
Rash maculo-papular	No. of Events (%)	26 (18.6)	4 (3.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.332 (1.861, 15.279)
	Treatment P-value [b]		0.00056
	Interaction P-value [c]		0.56300

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S7.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Any Event	No. of Events (%)	84 (98.8)	108 (99.1)
	Median Survival Est. (95% CI)	0.26 (0.16, 0.26)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.817 (0.614, 1.088)
	Treatment P-value [b]		0.11081
	Interaction P-value [c]		0.03090
Blood and lymphatic system disorders	No. of Events (%)	22 (25.9)	53 (48.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	12.94 (1.41, NC)
	Hazard Ratio (95% CI) [a]		0.405 (0.246, 0.666)
	Treatment P-value [b]		0.00029
	Interaction P-value [c]		0.00244

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Anaemia	No. of Events (%)	12 (14.1)	38 (34.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (12.94, NC)
	Hazard Ratio (95% CI) [a]		0.336 (0.176, 0.644)
	Treatment P-value [b]		0.00065
	Interaction P-value [c]		0.00105
Eye disorders	No. of Events (%)	22 (25.9)	15 (13.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.909 (0.990, 3.681)
	Treatment P-value [b]		0.05060
	Interaction P-value [c]		0.05831

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Dry eye	No. of Events (%)	5 (5.9)	2 (1.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.139 (0.609, 16.186)
	Treatment P-value [b]		0.14757
	Interaction P-value [c]		0.76374
Lacrimation increased	No. of Events (%)	6 (7.1)	10 (9.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.713 (0.259, 1.961)
	Treatment P-value [b]		0.47702
	Interaction P-value [c]		0.01021

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Diarrhoea	No. of Events (%)	24 (28.2)	34 (31.2)
	Median Survival Est. (95% CI)	NC (15.11, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.787 (0.467, 1.328)
	Treatment P-value [b]		0.37952
	Interaction P-value [c]		0.00461
Dry mouth	No. of Events (%)	3 (3.5)	4 (3.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.941 (0.211, 4.204)
	Treatment P-value [b]		0.91804
	Interaction P-value [c]		0.13877

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Chills	No. of Events (%)	5 (5.9)	2 (1.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.222 (0.625, 16.611)
	Treatment P-value [b]		0.13460
	Interaction P-value [c]		0.94074
Fatigue	No. of Events (%)	33 (38.8)	33 (30.3)
	Median Survival Est. (95% CI)	NC (6.93, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.202 (0.742, 1.947)
	Treatment P-value [b]		0.46594
	Interaction P-value [c]		0.33056

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Infections and infestations	No. of Events (%)	45 (52.9)	36 (33.0)
	Median Survival Est. (95% CI)	5.09 (2.56, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.714 (1.106, 2.658)
	Treatment P-value [b]		0.01681
	Interaction P-value [c]		0.59213
Conjunctivitis	No. of Events (%)	5 (5.9)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.01123
	Interaction P-value [c]		0.53991

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Date/time of run: 20APR2021 13:50
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Astellas: 7465-CL-0301
Table TEAE.KM.S7.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Alanine aminotransferase increased	No. of Events (%)	8 (9.4)	2 (1.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.287 (1.123, 24.898)
	Treatment P-value [b]		0.01807
	Interaction P-value [c]		0.69145
Aspartate aminotransferase increased	No. of Events (%)	11 (12.9)	3 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.858 (1.355, 17.415)
	Treatment P-value [b]		0.00694
	Interaction P-value [c]		0.66797

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Table TEAE.KM.S7.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Blood creatinine increased	No. of Events (%)	11 (12.9)	2 (1.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.242 (1.605, 32.675)
	Treatment P-value [b]		0.00275
	Interaction P-value [c]		0.54218
Neutrophil count decreased	No. of Events (%)	13 (15.3)	32 (29.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.414 (0.217, 0.788)
	Treatment P-value [b]		0.00974
	Interaction P-value [c]		0.27741

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Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Weight decreased	No. of Events (%)	16 (18.8)	4 (3.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.467 (1.828, 16.353)
	Treatment P-value [b]		0.00067
	Interaction P-value [c]		0.04747
White blood cell count decreased	No. of Events (%)	10 (11.8)	22 (20.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.504 (0.238, 1.064)
	Treatment P-value [b]		0.07672
	Interaction P-value [c]		0.94017

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Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Metabolism and nutrition disorders	No. of Events (%)	48 (56.5)	52 (47.7)
	Median Survival Est. (95% CI)	1.91 (0.76, NC)	NC (1.41, NC)
	Hazard Ratio (95% CI) [a]		1.221 (0.825, 1.808)
	Treatment P-value [b]		0.33309
	Interaction P-value [c]		0.00030
Decreased appetite	No. of Events (%)	30 (35.3)	30 (27.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.282 (0.773, 2.127)
	Treatment P-value [b]		0.34461
	Interaction P-value [c]		0.00209

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Hyperglycaemia	No. of Events (%)	10 (11.8)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00026
	Interaction P-value [c]		0.79581
Musculoskeletal and connective tissue disorders	No. of Events (%)	24 (28.2)	35 (32.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.798 (0.475, 1.342)
	Treatment P-value [b]		0.41575
	Interaction P-value [c]		0.68375

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Arthralgia	No. of Events (%)	5 (5.9)	8 (7.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.766 (0.251, 2.341)
	Treatment P-value [b]		0.65622
	Interaction P-value [c]		0.28933
Myalgia	No. of Events (%)	2 (2.4)	6 (5.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.406 (0.082, 2.011)
	Treatment P-value [b]		0.25348
	Interaction P-value [c]		0.97017

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Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Nervous system disorders	No. of Events (%)	59 (69.4)	48 (44.0)
	Median Survival Est. (95% CI)	2.73 (1.31, 3.71)	NC (3.45, NC)
	Hazard Ratio (95% CI) [a]		1.811 (1.237, 2.651)
	Treatment P-value [b]		0.00213
	Interaction P-value [c]		0.00007
Dysgeusia	No. of Events (%)	29 (34.1)	15 (13.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.680 (1.437, 5.000)
	Treatment P-value [b]		0.00149
	Interaction P-value [c]		0.23547

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Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Peripheral sensory neuropathy	No. of Events (%)	32 (37.6)	22 (20.2)
	Median Survival Est. (95% CI)	NC (5.13, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.869 (1.086, 3.217)
	Treatment P-value [b]		0.02334
	Interaction P-value [c]		0.00202
Renal and urinary disorders	No. of Events (%)	18 (21.2)	20 (18.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.159 (0.613, 2.192)
	Treatment P-value [b]		0.65830
	Interaction P-value [c]		0.28941

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Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Acute kidney injury	No. of Events (%)	3 (3.5)	4 (3.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.953 (0.213, 4.261)
	Treatment P-value [b]		0.95885
	Interaction P-value [c]		0.37645
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	33 (38.8)	22 (20.2)
	Median Survival Est. (95% CI)	NC (6.01, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.010 (1.172, 3.448)
	Treatment P-value [b]		0.00914
	Interaction P-value [c]		0.27993

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Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Skin and subcutaneous tissue disorders	No. of Events (%)	72 (84.7)	57 (52.3)
	Median Survival Est. (95% CI)	0.46 (0.36, 0.76)	3.42 (1.12, NC)
	Hazard Ratio (95% CI) [a]		2.588 (1.825, 3.669)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.00213
Drug eruption	No. of Events (%)	6 (7.1)	1 (0.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.954 (0.958, 66.070)
	Treatment P-value [b]		0.02266
	Interaction P-value [c]		0.89193

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Dry skin	No. of Events (%)	18 (21.2)	4 (3.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.227 (2.107, 18.401)
	Treatment P-value [b]		0.00014
	Interaction P-value [c]		0.29510
Pruritus	No. of Events (%)	31 (36.5)	8 (7.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.048 (2.779, 13.161)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.31160

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Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Rash	No. of Events (%)	16 (18.8)	8 (7.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.742 (1.174, 6.409)
	Treatment P-value [b]		0.01751
	Interaction P-value [c]		0.15527
Rash maculo-papular	No. of Events (%)	20 (23.5)	2 (1.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		14.227 (3.325, 60.877)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.56300

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System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Any Event	No. of Events (%)	69 (97.2)	74 (98.7)
	Median Survival Est. (95% CI)	0.20 (0.13, 0.26)	0.07 (0.07, 0.13)
	Hazard Ratio (95% CI) [a]		0.699 (0.503, 0.971)
	Treatment P-value [b]		0.04366
	Interaction P-value [c]		0.03090
Blood and lymphatic system disorders	No. of Events (%)	20 (28.2)	41 (54.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	2.76 (1.38, NC)
	Hazard Ratio (95% CI) [a]		0.384 (0.225, 0.656)
	Treatment P-value [b]		0.00037
	Interaction P-value [c]		0.00244

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Astellas: 7465-CL-0301
Table TEAE.KM.S7.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Anaemia	No. of Events (%)	13 (18.3)	30 (40.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (3.52, NC)
	Hazard Ratio (95% CI) [a]		0.398 (0.208, 0.764)
	Treatment P-value [b]		0.00347
	Interaction P-value [c]		0.00105
Eye disorders	No. of Events (%)	23 (32.4)	3 (4.0)
	Median Survival Est. (95% CI)	NC (8.80, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.615 (2.887, 32.028)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.05831

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Dry eye	No. of Events (%)	3 (4.2)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.07311
	Interaction P-value [c]		0.76374
Lacrimation increased	No. of Events (%)	9 (12.7)	1 (1.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		10.202 (1.292, 80.526)
	Treatment P-value [b]		0.00736
	Interaction P-value [c]		0.01021

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Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Diarrhoea	No. of Events (%)	31 (43.7)	15 (20.0)
	Median Survival Est. (95% CI)	NC (2.40, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.572 (1.388, 4.765)
	Treatment P-value [b]		0.00148
	Interaction P-value [c]		0.00461
Dry mouth	No. of Events (%)	8 (11.3)	2 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.511 (0.958, 21.247)
	Treatment P-value [b]		0.03966
	Interaction P-value [c]		0.13877

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Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Chills	No. of Events (%)	3 (4.2)	1 (1.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.193 (0.332, 30.685)
	Treatment P-value [b]		0.30462
	Interaction P-value [c]		0.94074
Fatigue	No. of Events (%)	19 (26.8)	9 (12.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.333 (1.055, 5.157)
	Treatment P-value [b]		0.03087
	Interaction P-value [c]		0.33056

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Infections and infestations	No. of Events (%)	38 (53.5)	27 (36.0)
	Median Survival Est. (95% CI)	4.40 (2.20, NC)	NC (10.41, NC)
	Hazard Ratio (95% CI) [a]		1.662 (1.015, 2.723)
	Treatment P-value [b]		0.04307
	Interaction P-value [c]		0.59213
Conjunctivitis	No. of Events (%)	11 (15.5)	1 (1.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		12.545 (1.619, 97.183)
	Treatment P-value [b]		0.00210
	Interaction P-value [c]		0.53991

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Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Alanine aminotransferase increased	No. of Events (%)	6 (8.5)	2 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.260 (0.658, 16.154)
	Treatment P-value [b]		0.13108
	Interaction P-value [c]		0.69145
Aspartate aminotransferase increased	No. of Events (%)	7 (9.9)	1 (1.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.574 (0.932, 61.563)
	Treatment P-value [b]		0.02723
	Interaction P-value [c]		0.66797

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Blood creatinine increased	No. of Events (%)	5 (7.0)	2 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.671 (0.518, 13.767)
	Treatment P-value [b]		0.21910
	Interaction P-value [c]		0.54218
Neutrophil count decreased	No. of Events (%)	4 (5.6)	9 (12.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.449 (0.138, 1.457)
	Treatment P-value [b]		0.14702
	Interaction P-value [c]		0.27741

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Weight decreased	No. of Events (%)	8 (11.3)	9 (12.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.921 (0.355, 2.386)
	Treatment P-value [b]		0.83416
	Interaction P-value [c]		0.04747
White blood cell count decreased	No. of Events (%)	1 (1.4)	3 (4.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.337 (0.035, 3.241)
	Treatment P-value [b]		0.31875
	Interaction P-value [c]		0.94017

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System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Metabolism and nutrition disorders	No. of Events (%)	39 (54.9)	43 (57.3)
	Median Survival Est. (95% CI)	2.14 (1.31, NC)	2.33 (0.69, NC)
	Hazard Ratio (95% CI) [a]		0.807 (0.523, 1.244)
	Treatment P-value [b]		0.36538
	Interaction P-value [c]		0.00030
Decreased appetite	No. of Events (%)	30 (42.3)	32 (42.7)
	Median Survival Est. (95% CI)	NC (2.79, NC)	NC (2.79, NC)
	Hazard Ratio (95% CI) [a]		0.896 (0.544, 1.474)
	Treatment P-value [b]		0.69050
	Interaction P-value [c]		0.00209

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System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Hyperglycaemia	No. of Events (%)	9 (12.7)	4 (5.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.429 (0.748, 7.889)
	Treatment P-value [b]		0.12045
	Interaction P-value [c]		0.79581
Musculoskeletal and connective tissue disorders	No. of Events (%)	23 (32.4)	33 (44.0)
	Median Survival Est. (95% CI)	NC (6.60, NC)	8.02 (3.02, NC)
	Hazard Ratio (95% CI) [a]		0.653 (0.383, 1.111)
	Treatment P-value [b]		0.10030
	Interaction P-value [c]		0.68375

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Arthralgia	No. of Events (%)	5 (7.0)	7 (9.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.737 (0.234, 2.323)
	Treatment P-value [b]		0.58144
	Interaction P-value [c]		0.28933
Myalgia	No. of Events (%)	4 (5.6)	9 (12.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.448 (0.138, 1.455)
	Treatment P-value [b]		0.16943
	Interaction P-value [c]		0.97017

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System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Nervous system disorders	No. of Events (%)	43 (60.6)	22 (29.3)
	Median Survival Est. (95% CI)	2.43 (1.87, 3.94)	NC (8.61, NC)
	Hazard Ratio (95% CI) [a]		2.824 (1.688, 4.726)
	Treatment P-value [b]		0.00004
	Interaction P-value [c]		0.00007
Dysgeusia	No. of Events (%)	14 (19.7)	5 (6.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.258 (1.173, 9.046)
	Treatment P-value [b]		0.01663
	Interaction P-value [c]		0.23547

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Peripheral sensory neuropathy	No. of Events (%)	15 (21.1)	3 (4.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.863 (1.697, 20.252)
	Treatment P-value [b]		0.00156
	Interaction P-value [c]		0.00202
Renal and urinary disorders	No. of Events (%)	17 (23.9)	16 (21.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.082 (0.547, 2.142)
	Treatment P-value [b]		0.85103
	Interaction P-value [c]		0.28941

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Table TEAE.KM.S7.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Acute kidney injury	No. of Events (%)	5 (7.0)	2 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.624 (0.509, 13.526)
	Treatment P-value [b]		0.24005
	Interaction P-value [c]		0.37645
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	20 (28.2)	14 (18.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.579 (0.797, 3.126)
	Treatment P-value [b]		0.19371
	Interaction P-value [c]		0.27993

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table TEAE.KM.S7.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Skin and subcutaneous tissue disorders	No. of Events (%)	52 (73.2)	22 (29.3)
	Median Survival Est. (95% CI)	0.95 (0.66, 1.22)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.595 (2.181, 5.925)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.00213
Drug eruption	No. of Events (%)	3 (4.2)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.07202
	Interaction P-value [c]		0.89193

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S7.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Dry skin	No. of Events (%)	11 (15.5)	1 (1.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		12.473 (1.612, 96.517)
	Treatment P-value [b]		0.00194
	Interaction P-value [c]		0.29510
Pruritus	No. of Events (%)	18 (25.4)	1 (1.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		22.232 (2.969, 166.496)
	Treatment P-value [b]		0.00002
	Interaction P-value [c]		0.31160

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S7.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Rash	No. of Events (%)	17 (23.9)	2 (2.7)
	Median Survival Est. (95% CI)	NC (12.68, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		10.045 (2.320, 43.486)
	Treatment P-value [b]		0.00013
	Interaction P-value [c]		0.15527
Rash maculo-papular	No. of Events (%)	4 (5.6)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.04228
	Interaction P-value [c]		0.56300

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Analysis Plan: 15FEB2021 Confidential

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Table TEAE.KM.S8.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Any Event	No. of Events (%)	95 (99.0)	101 (99.0)
	Median Survival Est. (95% CI)	0.21 (0.16, 0.26)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.816 (0.616, 1.080)
	Treatment P-value [b]		0.12389
	Interaction P-value [c]		0.31329
Blood and lymphatic system disorders	No. of Events (%)	31 (32.3)	42 (41.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (5.36, NC)
	Hazard Ratio (95% CI) [a]		0.672 (0.422, 1.069)
	Treatment P-value [b]		0.09855
	Interaction P-value [c]		0.43126

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S8.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Anaemia	No. of Events (%)	23 (24.0)	27 (26.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.862 (0.494, 1.503)
	Treatment P-value [b]		0.62423
	Interaction P-value [c]		0.15264
Febrile neutropenia	No. of Events (%)	3 (3.1)	7 (6.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.440 (0.114, 1.703)
	Treatment P-value [b]		0.22070
	Interaction P-value [c]		0.24274

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S8.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Eye disorders	No. of Events (%)	26 (27.1)	10 (9.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.986 (1.440, 6.193)
	Treatment P-value [b]		0.00206
	Interaction P-value [c]		0.73628
Dry eye	No. of Events (%)	8 (8.3)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00313
	Interaction P-value [c]		0.98906

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S8.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Lacrimation increased	No. of Events (%)	6 (6.3)	3 (2.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.127 (0.532, 8.504)
	Treatment P-value [b]		0.28585
	Interaction P-value [c]		0.84220
Vision blurred	No. of Events (%)	2 (2.1)	3 (2.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.689 (0.115, 4.122)
	Treatment P-value [b]		0.68832
	Interaction P-value [c]		0.05695

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S8.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Diarrhoea	No. of Events (%)	29 (30.2)	24 (23.5)
	Median Survival Est. (95% CI)	NC (15.11, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.303 (0.759, 2.239)
	Treatment P-value [b]		0.32870
	Interaction P-value [c]		0.44032
Dry mouth	No. of Events (%)	9 (9.4)	2 (2.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.904 (1.060, 22.696)
	Treatment P-value [b]		0.02626
	Interaction P-value [c]		0.57196

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S8.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Chills	No. of Events (%)	5 (5.2)	2 (2.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.695 (0.523, 13.893)
	Treatment P-value [b]		0.22208
	Interaction P-value [c]		0.95803
Fatigue	No. of Events (%)	31 (32.3)	30 (29.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.050 (0.636, 1.735)
	Treatment P-value [b]		0.86430
	Interaction P-value [c]		0.20041

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Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Infections and infestations	No. of Events (%)	42 (43.8)	31 (30.4)
	Median Survival Est. (95% CI)	NC (3.48, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.485 (0.934, 2.363)
	Treatment P-value [b]		0.11678
	Interaction P-value [c]		0.93368
Conjunctivitis	No. of Events (%)	4 (4.2)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.04534
	Interaction P-value [c]		0.99064

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Alanine aminotransferase increased	No. of Events (%)	8 (8.3)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00338
	Interaction P-value [c]		0.98676
Aspartate aminotransferase increased	No. of Events (%)	10 (10.4)	1 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		11.104 (1.422, 86.714)
	Treatment P-value [b]		0.00432
	Interaction P-value [c]		0.63473

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Blood creatinine increased	No. of Events (%)	6 (6.3)	3 (2.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.152 (0.538, 8.606)
	Treatment P-value [b]		0.26647
	Interaction P-value [c]		0.37098
Neutrophil count decreased	No. of Events (%)	15 (15.6)	22 (21.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.650 (0.337, 1.253)
	Treatment P-value [b]		0.19925
	Interaction P-value [c]		0.47981

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Weight decreased	No. of Events (%)	14 (14.6)	7 (6.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.136 (0.862, 5.292)
	Treatment P-value [b]		0.09453
	Interaction P-value [c]		0.73501
White blood cell count decreased	No. of Events (%)	6 (6.3)	12 (11.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.492 (0.185, 1.311)
	Treatment P-value [b]		0.15231
	Interaction P-value [c]		0.84986

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Date/time of run: 20APR2021 13:50
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Astellas: 7465-CL-0301
Table TEAE.KM.S8.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Metabolism and nutrition disorders	No. of Events (%)	60 (62.5)	46 (45.1)
	Median Survival Est. (95% CI)	2.04 (1.02, 5.06)	NC (1.45, NC)
	Hazard Ratio (95% CI) [a]		1.426 (0.971, 2.094)
	Treatment P-value [b]		0.06989
	Interaction P-value [c]		0.95290
Decreased appetite	No. of Events (%)	41 (42.7)	28 (27.5)
	Median Survival Est. (95% CI)	NC (5.06, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.541 (0.953, 2.491)
	Treatment P-value [b]		0.07464
	Interaction P-value [c]		0.94200

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S8.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Hyperglycaemia	No. of Events (%)	11 (11.5)	4 (3.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.993 (0.953, 9.402)
	Treatment P-value [b]		0.05073
	Interaction P-value [c]		0.20948
Musculoskeletal and connective tissue disorders	No. of Events (%)	30 (31.3)	42 (41.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (4.30, NC)
	Hazard Ratio (95% CI) [a]		0.628 (0.393, 1.004)
	Treatment P-value [b]		0.05086
	Interaction P-value [c]		0.57784

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Table TEAE.KM.S8.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Arthralgia	No. of Events (%)	4 (4.2)	14 (13.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.274 (0.090, 0.833)
	Treatment P-value [b]		0.01436
	Interaction P-value [c]		0.19463
Myalgia	No. of Events (%)	1 (1.0)	9 (8.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.113 (0.014, 0.894)
	Treatment P-value [b]		0.01267
	Interaction P-value [c]		0.15893

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Table TEAE.KM.S8.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Nervous system disorders	No. of Events (%)	66 (68.8)	50 (49.0)
	Median Survival Est. (95% CI)	2.73 (1.68, 3.42)	4.60 (2.79, NC)
	Hazard Ratio (95% CI) [a]		1.489 (1.031, 2.152)
	Treatment P-value [b]		0.02534
	Interaction P-value [c]		0.88420
Dysgeusia	No. of Events (%)	26 (27.1)	9 (8.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.256 (1.525, 6.949)
	Treatment P-value [b]		0.00110
	Interaction P-value [c]		0.86835

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Table TEAE.KM.S8.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Peripheral sensory neuropathy	No. of Events (%)	40 (41.7)	27 (26.5)
	Median Survival Est. (95% CI)	NC (4.93, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.567 (0.962, 2.554)
	Treatment P-value [b]		0.06712
	Interaction P-value [c]		0.75354
Renal and urinary disorders	No. of Events (%)	21 (21.9)	15 (14.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.565 (0.807, 3.036)
	Treatment P-value [b]		0.18876
	Interaction P-value [c]		0.76263

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Table TEAE.KM.S8.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Acute kidney injury	No. of Events (%)	5 (5.2)	2 (2.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.661 (0.516, 13.714)
	Treatment P-value [b]		0.23106
	Interaction P-value [c]		0.84247
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	30 (31.3)	20 (19.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.626 (0.924, 2.864)
	Treatment P-value [b]		0.08692
	Interaction P-value [c]		0.73274

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Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Skin and subcutaneous tissue disorders	No. of Events (%)	84 (87.5)	61 (59.8)
	Median Survival Est. (95% CI)	0.48 (0.36, 0.72)	0.95 (0.72, 5.13)
	Hazard Ratio (95% CI) [a]		2.135 (1.533, 2.973)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.85509
Blister	No. of Events (%)	0	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		NA
	Interaction P-value [c]		0.99941

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Table TEAE.KM.S8.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Drug eruption	No. of Events (%)	9 (9.4)	2 (2.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.824 (1.042, 22.328)
	Treatment P-value [b]		0.02537
	Interaction P-value [c]		0.61903
Dry skin	No. of Events (%)	15 (15.6)	3 (2.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.641 (1.633, 19.487)
	Treatment P-value [b]		0.00200
	Interaction P-value [c]		0.72564

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Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Pruritus	No. of Events (%)	38 (39.6)	8 (7.8)
	Median Survival Est. (95% CI)	NC (5.55, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.272 (2.925, 13.447)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.92084
Rash	No. of Events (%)	17 (17.7)	7 (6.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.697 (1.118, 6.503)
	Treatment P-value [b]		0.02444
	Interaction P-value [c]		0.72885

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Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Rash maculo-papular	No. of Events (%)	21 (21.9)	3 (2.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		8.223 (2.452, 27.572)
	Treatment P-value [b]		0.00005
	Interaction P-value [c]		0.85636
Skin hyperpigmentation	No. of Events (%)	7 (7.3)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00563
	Interaction P-value [c]		0.99082

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Table TEAE.KM.S8.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Any Event	No. of Events (%)	195 (97.5)	187 (98.9)
	Median Survival Est. (95% CI)	0.16 (0.13, 0.23)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.974 (0.796, 1.191)
	Treatment P-value [b]		0.86836
	Interaction P-value [c]		0.31329
Blood and lymphatic system disorders	No. of Events (%)	54 (27.0)	81 (42.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (4.90, NC)
	Hazard Ratio (95% CI) [a]		0.533 (0.378, 0.752)
	Treatment P-value [b]		0.00024
	Interaction P-value [c]		0.43126

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Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Anaemia	No. of Events (%)	37 (18.5)	60 (31.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.520 (0.345, 0.784)
	Treatment P-value [b]		0.00132
	Interaction P-value [c]		0.15264
Febrile neutropenia	No. of Events (%)	1 (0.5)	9 (4.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.101 (0.013, 0.798)
	Treatment P-value [b]		0.00754
	Interaction P-value [c]		0.24274

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Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Eye disorders	No. of Events (%)	54 (27.0)	16 (8.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.497 (2.001, 6.109)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.73628
Dry eye	No. of Events (%)	11 (5.5)	3 (1.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.407 (0.950, 12.215)
	Treatment P-value [b]		0.04991
	Interaction P-value [c]		0.98906

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Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Lacrimation increased	No. of Events (%)	24 (12.0)	9 (4.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.498 (1.161, 5.375)
	Treatment P-value [b]		0.01475
	Interaction P-value [c]		0.84220
Vision blurred	No. of Events (%)	14 (7.0)	2 (1.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.575 (1.494, 28.932)
	Treatment P-value [b]		0.00413
	Interaction P-value [c]		0.05695

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table TEAE.KM.S8.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Diarrhoea	No. of Events (%)	74 (37.0)	43 (22.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.689 (1.160, 2.460)
	Treatment P-value [b]		0.00594
	Interaction P-value [c]		0.44032
Dry mouth	No. of Events (%)	15 (7.5)	5 (2.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.888 (1.050, 7.947)
	Treatment P-value [b]		0.03153
	Interaction P-value [c]		0.57196

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S8.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Chills	No. of Events (%)	12 (6.0)	4 (2.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.844 (0.917, 8.818)
	Treatment P-value [b]		0.05941
	Interaction P-value [c]		0.95803
Fatigue	No. of Events (%)	77 (38.5)	48 (25.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.573 (1.097, 2.255)
	Treatment P-value [b]		0.01213
	Interaction P-value [c]		0.20041

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Table TEAE.KM.S8.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Infections and infestations	No. of Events (%)	110 (55.0)	74 (39.2)
	Median Survival Est. (95% CI)	3.94 (3.06, 9.03)	NC (7.56, NC)
	Hazard Ratio (95% CI) [a]		1.520 (1.132, 2.042)
	Treatment P-value [b]		0.00445
	Interaction P-value [c]		0.93368
Conjunctivitis	No. of Events (%)	15 (7.5)	2 (1.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.121 (1.628, 31.143)
	Treatment P-value [b]		0.00215
	Interaction P-value [c]		0.99064

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Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Alanine aminotransferase increased	No. of Events (%)	19 (9.5)	5 (2.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.656 (1.365, 9.792)
	Treatment P-value [b]		0.00567
	Interaction P-value [c]		0.98676
Aspartate aminotransferase increased	No. of Events (%)	26 (13.0)	4 (2.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.345 (2.214, 18.181)
	Treatment P-value [b]		0.00007
	Interaction P-value [c]		0.63473

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S8.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Blood creatinine increased	No. of Events (%)	20 (10.0)	4 (2.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.791 (1.637, 14.018)
	Treatment P-value [b]		0.00160
	Interaction P-value [c]		0.37098
Neutrophil count decreased	No. of Events (%)	18 (9.0)	32 (16.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.474 (0.266, 0.845)
	Treatment P-value [b]		0.01037
	Interaction P-value [c]		0.47981

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Weight decreased	No. of Events (%)	34 (17.0)	13 (6.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.587 (1.365, 4.903)
	Treatment P-value [b]		0.00234
	Interaction P-value [c]		0.73501
White blood cell count decreased	No. of Events (%)	10 (5.0)	20 (10.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.436 (0.204, 0.932)
	Treatment P-value [b]		0.02884
	Interaction P-value [c]		0.84986

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Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Metabolism and nutrition disorders	No. of Events (%)	114 (57.0)	80 (42.3)
	Median Survival Est. (95% CI)	2.53 (1.41, 6.67)	NC (6.05, NC)
	Hazard Ratio (95% CI) [a]		1.446 (1.087, 1.926)
	Treatment P-value [b]		0.01203
	Interaction P-value [c]		0.95290
Decreased appetite	No. of Events (%)	80 (40.0)	50 (26.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.575 (1.106, 2.243)
	Treatment P-value [b]		0.01189
	Interaction P-value [c]		0.94200

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Hyperglycaemia	No. of Events (%)	20 (10.0)	2 (1.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.786 (2.288, 41.865)
	Treatment P-value [b]		0.00015
	Interaction P-value [c]		0.20948
Musculoskeletal and connective tissue disorders	No. of Events (%)	70 (35.0)	78 (41.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (7.59, NC)
	Hazard Ratio (95% CI) [a]		0.739 (0.535, 1.020)
	Treatment P-value [b]		0.06711
	Interaction P-value [c]		0.57784

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Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Arthralgia	No. of Events (%)	16 (8.0)	22 (11.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.641 (0.337, 1.221)
	Treatment P-value [b]		0.17268
	Interaction P-value [c]		0.19463
Myalgia	No. of Events (%)	14 (7.0)	23 (12.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.539 (0.277, 1.048)
	Treatment P-value [b]		0.06574
	Interaction P-value [c]		0.15893

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Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Nervous system disorders	No. of Events (%)	123 (61.5)	87 (46.0)
	Median Survival Est. (95% CI)	2.99 (2.07, 4.07)	7.66 (3.94, NC)
	Hazard Ratio (95% CI) [a]		1.439 (1.094, 1.894)
	Treatment P-value [b]		0.01030
	Interaction P-value [c]		0.88420
Dysgeusia	No. of Events (%)	48 (24.0)	14 (7.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.532 (1.947, 6.407)
	Treatment P-value [b]		0.00001
	Interaction P-value [c]		0.86835

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Peripheral sensory neuropathy	No. of Events (%)	62 (31.0)	39 (20.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.417 (0.949, 2.115)
	Treatment P-value [b]		0.08693
	Interaction P-value [c]		0.75354
Renal and urinary disorders	No. of Events (%)	54 (27.0)	37 (19.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.387 (0.913, 2.108)
	Treatment P-value [b]		0.11911
	Interaction P-value [c]		0.76263

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Table TEAE.KM.S8.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Acute kidney injury	No. of Events (%)	14 (7.0)	6 (3.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.195 (0.843, 5.713)
	Treatment P-value [b]		0.09426
	Interaction P-value [c]		0.84247
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	71 (35.5)	48 (25.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.446 (1.003, 2.086)
	Treatment P-value [b]		0.04737
	Interaction P-value [c]		0.73274

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Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Skin and subcutaneous tissue disorders	No. of Events (%)	153 (76.5)	89 (47.1)
	Median Survival Est. (95% CI)	0.79 (0.53, 0.95)	NC (2.10, NC)
	Hazard Ratio (95% CI) [a]		2.220 (1.708, 2.886)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.85509
Blister	No. of Events (%)	9 (4.5)	1 (0.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		8.143 (1.031, 64.298)
	Treatment P-value [b]		0.01761
	Interaction P-value [c]		0.99941

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[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Astellas: 7465-CL-0301
Table TEAE.KM.S8.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Drug eruption	No. of Events (%)	17 (8.5)	2 (1.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		8.260 (1.908, 35.753)
	Treatment P-value [b]		0.00077
	Interaction P-value [c]		0.61903
Dry skin	No. of Events (%)	35 (17.5)	8 (4.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.345 (2.015, 9.366)
	Treatment P-value [b]		0.00004
	Interaction P-value [c]		0.72564

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S8.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Pruritus	No. of Events (%)	64 (32.0)	12 (6.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.968 (3.221, 11.057)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.92084
Rash	No. of Events (%)	33 (16.5)	10 (5.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.293 (1.623, 6.682)
	Treatment P-value [b]		0.00046
	Interaction P-value [c]		0.72885

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Table TEAE.KM.S8.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Rash maculo-papular	No. of Events (%)	29 (14.5)	3 (1.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.617 (2.930, 31.573)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.85636
Skin hyperpigmentation	No. of Events (%)	12 (6.0)	1 (0.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		11.621 (1.511, 89.371)
	Treatment P-value [b]		0.00278
	Interaction P-value [c]		0.99082

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Table TEAE.KM.S9.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Any Event	No. of Events (%)	253 (97.7)	252 (98.8)
	Median Survival Est. (95% CI)	0.20 (0.16, 0.23)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.935 (0.784, 1.113)
	Treatment P-value [b]		0.47745
	Interaction P-value [c]		0.54679
Blood and lymphatic system disorders	No. of Events (%)	78 (30.1)	109 (42.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (5.68, NC)
	Hazard Ratio (95% CI) [a]		0.597 (0.446, 0.798)
	Treatment P-value [b]		0.00042
	Interaction P-value [c]		0.46915

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S9.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Anaemia	No. of Events (%)	55 (21.2)	75 (29.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.664 (0.469, 0.940)
	Treatment P-value [b]		0.02000
	Interaction P-value [c]		0.25815
Febrile neutropenia	No. of Events (%)	4 (1.5)	15 (5.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.253 (0.084, 0.762)
	Treatment P-value [b]		0.00831
	Interaction P-value [c]		0.99066

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Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Eye disorders	No. of Events (%)	74 (28.6)	22 (8.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.674 (2.283, 5.915)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.17282
Dry eye	No. of Events (%)	18 (6.9)	2 (0.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		8.875 (2.059, 38.253)
	Treatment P-value [b]		0.00038
	Interaction P-value [c]		0.16119

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Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Lacrimation increased	No. of Events (%)	30 (11.6)	11 (4.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.709 (1.358, 5.406)
	Treatment P-value [b]		0.00325
	Interaction P-value [c]		0.98388
Vision blurred	No. of Events (%)	14 (5.4)	5 (2.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.730 (0.983, 7.580)
	Treatment P-value [b]		0.04404
	Interaction P-value [c]		0.98959

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Diarrhoea	No. of Events (%)	92 (35.5)	62 (24.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.507 (1.092, 2.081)
	Treatment P-value [b]		0.01224
	Interaction P-value [c]		0.50609
Dry mouth	No. of Events (%)	22 (8.5)	6 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.696 (1.498, 9.115)
	Treatment P-value [b]		0.00241
	Interaction P-value [c]		0.62458

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Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Chills	No. of Events (%)	15 (5.8)	6 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.477 (0.961, 6.386)
	Treatment P-value [b]		0.05229
	Interaction P-value [c]		0.98891
Fatigue	No. of Events (%)	96 (37.1)	70 (27.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.356 (0.997, 1.846)
	Treatment P-value [b]		0.05060
	Interaction P-value [c]		0.81025

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Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Infections and infestations	No. of Events (%)	131 (50.6)	90 (35.3)
	Median Survival Est. (95% CI)	6.57 (3.48, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.519 (1.161, 1.987)
	Treatment P-value [b]		0.00205
	Interaction P-value [c]		0.99090
Conjunctivitis	No. of Events (%)	15 (5.8)	2 (0.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.350 (1.681, 32.147)
	Treatment P-value [b]		0.00175
	Interaction P-value [c]		0.99115

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Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Alanine aminotransferase increased	No. of Events (%)	21 (8.1)	4 (1.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.255 (1.804, 15.310)
	Treatment P-value [b]		0.00068
	Interaction P-value [c]		0.87798
Aspartate aminotransferase increased	No. of Events (%)	31 (12.0)	4 (1.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.888 (2.784, 22.348)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.72746

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Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Blood creatinine increased	No. of Events (%)	24 (9.3)	7 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.433 (1.479, 7.969)
	Treatment P-value [b]		0.00218
	Interaction P-value [c]		0.98776
Neutrophil count decreased	No. of Events (%)	24 (9.3)	48 (18.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.435 (0.266, 0.710)
	Treatment P-value [b]		0.00064
	Interaction P-value [c]		0.04261

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Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Weight decreased	No. of Events (%)	43 (16.6)	20 (7.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.173 (1.279, 3.694)
	Treatment P-value [b]		0.00325
	Interaction P-value [c]		0.98038
White blood cell count decreased	No. of Events (%)	10 (3.9)	29 (11.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.312 (0.152, 0.640)
	Treatment P-value [b]		0.00087
	Interaction P-value [c]		0.02432

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Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Metabolism and nutrition disorders	No. of Events (%)	155 (59.8)	107 (42.0)
	Median Survival Est. (95% CI)	2.14 (1.41, 4.11)	NC (7.23, NC)
	Hazard Ratio (95% CI) [a]		1.539 (1.203, 1.970)
	Treatment P-value [b]		0.00053
	Interaction P-value [c]		0.11350
Decreased appetite	No. of Events (%)	106 (40.9)	67 (26.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.595 (1.175, 2.166)
	Treatment P-value [b]		0.00247
	Interaction P-value [c]		0.70581

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Astellas: 7465-CL-0301
Table TEAE.KM.S9.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Hyperglycaemia	No. of Events (%)	29 (11.2)	6 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.914 (2.040, 11.837)
	Treatment P-value [b]		0.00008
	Interaction P-value [c]		0.98776
Musculoskeletal and connective tissue disorders	No. of Events (%)	86 (33.2)	105 (41.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (7.59, NC)
	Hazard Ratio (95% CI) [a]		0.681 (0.512, 0.906)
	Treatment P-value [b]		0.00836
	Interaction P-value [c]		0.55862

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Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Arthralgia	No. of Events (%)	18 (6.9)	31 (12.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.526 (0.294, 0.940)
	Treatment P-value [b]		0.02732
	Interaction P-value [c]		0.68631
Myalgia	No. of Events (%)	14 (5.4)	28 (11.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.466 (0.245, 0.885)
	Treatment P-value [b]		0.01700
	Interaction P-value [c]		0.54040

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Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Nervous system disorders	No. of Events (%)	163 (62.9)	120 (47.1)
	Median Survival Est. (95% CI)	2.83 (2.14, 3.71)	6.93 (3.94, NC)
	Hazard Ratio (95% CI) [a]		1.433 (1.132, 1.814)
	Treatment P-value [b]		0.00260
	Interaction P-value [c]		0.74954
Dysgeusia	No. of Events (%)	65 (25.1)	19 (7.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.646 (2.187, 6.080)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.49469

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Table TEAE.KM.S9.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Peripheral motor neuropathy	No. of Events (%)	10 (3.9)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00311
	Interaction P-value [c]		0.99995
Peripheral sensory neuropathy	No. of Events (%)	87 (33.6)	58 (22.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.406 (1.009, 1.960)
	Treatment P-value [b]		0.04319
	Interaction P-value [c]		0.56964

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Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Taste disorder	No. of Events (%)	11 (4.2)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00091
	Interaction P-value [c]		0.99808
Renal and urinary disorders	No. of Events (%)	68 (26.3)	45 (17.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.518 (1.042, 2.212)
	Treatment P-value [b]		0.02823
	Interaction P-value [c]		0.46548

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Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Acute kidney injury	No. of Events (%)	18 (6.9)	7 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.517 (1.051, 6.029)
	Treatment P-value [b]		0.03205
	Interaction P-value [c]		0.53118
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	90 (34.7)	61 (23.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.496 (1.081, 2.071)
	Treatment P-value [b]		0.01453
	Interaction P-value [c]		0.90500

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Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Skin and subcutaneous tissue disorders	No. of Events (%)	210 (81.1)	130 (51.0)
	Median Survival Est. (95% CI)	0.62 (0.49, 0.82)	3.25 (1.41, NC)
	Hazard Ratio (95% CI) [a]		2.247 (1.803, 2.800)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.26671
Drug eruption	No. of Events (%)	24 (9.3)	1 (0.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		24.267 (3.283, 179.382)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.00787

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Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Dry skin	No. of Events (%)	47 (18.1)	11 (4.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.459 (2.313, 8.598)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.98411
Pruritus	No. of Events (%)	91 (35.1)	17 (6.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.318 (3.763, 10.607)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.59749

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Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Rash	No. of Events (%)	45 (17.4)	14 (5.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.337 (1.832, 6.080)
	Treatment P-value [b]		0.00003
	Interaction P-value [c]		0.38509
Rash maculo-papular	No. of Events (%)	44 (17.0)	6 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.707 (3.284, 18.086)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.98489

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Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Skin hyperpigmentation	No. of Events (%)	17 (6.6)	1 (0.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		17.254 (2.296, 129.649)
	Treatment P-value [b]		0.00014
	Interaction P-value [c]		0.99195

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Table TEAE.KM.S9.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Any Event	No. of Events (%)	37 (100.0)	36 (100.0)
	Median Survival Est. (95% CI)	0.23 (0.13, 0.26)	0.13 (0.10, 0.20)
	Hazard Ratio (95% CI) [a]		0.804 (0.508, 1.272)
	Treatment P-value [b]		0.18733
	Interaction P-value [c]		0.54679
Blood and lymphatic system disorders	No. of Events (%)	7 (18.9)	14 (38.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	12.94 (2.14, NC)
	Hazard Ratio (95% CI) [a]		0.420 (0.169, 1.040)
	Treatment P-value [b]		0.06369
	Interaction P-value [c]		0.46915

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Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Anaemia	No. of Events (%)	5 (13.5)	12 (33.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (12.94, NC)
	Hazard Ratio (95% CI) [a]		0.352 (0.124, 0.999)
	Treatment P-value [b]		0.04987
	Interaction P-value [c]		0.25815
Febrile neutropenia	No. of Events (%)	0	1 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.31068
	Interaction P-value [c]		0.99066

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Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Eye disorders	No. of Events (%)	6 (16.2)	4 (11.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.435 (0.405, 5.085)
	Treatment P-value [b]		0.57291
	Interaction P-value [c]		0.17282
Dry eye	No. of Events (%)	1 (2.7)	1 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.945 (0.059, 15.109)
	Treatment P-value [b]		0.88978
	Interaction P-value [c]		0.16119

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Astellas: 7465-CL-0301
Table TEAE.KM.S9.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Lacrimation increased	No. of Events (%)	0	1 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.31030
	Interaction P-value [c]		0.98388
Vision blurred	No. of Events (%)	2 (5.4)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.18231
	Interaction P-value [c]		0.98959

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Analysis Plan: 15FEB2021 Confidential

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Table TEAE.KM.S9.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Diarrhoea	No. of Events (%)	11 (29.7)	5 (13.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.193 (0.762, 6.312)
	Treatment P-value [b]		0.14161
	Interaction P-value [c]		0.50609
Dry mouth	No. of Events (%)	2 (5.4)	1 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.948 (0.177, 21.484)
	Treatment P-value [b]		0.55223
	Interaction P-value [c]		0.62458

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Chills	No. of Events (%)	2 (5.4)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.16014
	Interaction P-value [c]		0.98891
Fatigue	No. of Events (%)	12 (32.4)	8 (22.2)
	Median Survival Est. (95% CI)	NC (4.40, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.523 (0.623, 3.726)
	Treatment P-value [b]		0.36169
	Interaction P-value [c]		0.81025

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Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Infections and infestations	No. of Events (%)	21 (56.8)	15 (41.7)
	Median Survival Est. (95% CI)	3.94 (1.87, NC)	NC (2.92, NC)
	Hazard Ratio (95% CI) [a]		1.513 (0.780, 2.935)
	Treatment P-value [b]		0.22275
	Interaction P-value [c]		0.99090
Conjunctivitis	No. of Events (%)	4 (10.8)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.04030
	Interaction P-value [c]		0.99115

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Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Alanine aminotransferase increased	No. of Events (%)	6 (16.2)	1 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.328 (0.762, 52.569)
	Treatment P-value [b]		0.04980
	Interaction P-value [c]		0.87798
Aspartate aminotransferase increased	No. of Events (%)	5 (13.5)	1 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.161 (0.603, 44.177)
	Treatment P-value [b]		0.09368
	Interaction P-value [c]		0.72746

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Blood creatinine increased	No. of Events (%)	2 (5.4)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.19137
	Interaction P-value [c]		0.98776
Neutrophil count decreased	No. of Events (%)	9 (24.3)	6 (16.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.418 (0.505, 3.985)
	Treatment P-value [b]		0.52070
	Interaction P-value [c]		0.04261

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Weight decreased	No. of Events (%)	5 (13.5)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.02236
	Interaction P-value [c]		0.98038
White blood cell count decreased	No. of Events (%)	6 (16.2)	3 (8.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.875 (0.469, 7.499)
	Treatment P-value [b]		0.35977
	Interaction P-value [c]		0.02432

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Metabolism and nutrition disorders	No. of Events (%)	19 (51.4)	19 (52.8)
	Median Survival Est. (95% CI)	3.06 (0.82, NC)	1.74 (0.69, NC)
	Hazard Ratio (95% CI) [a]		0.887 (0.470, 1.676)
	Treatment P-value [b]		0.74820
	Interaction P-value [c]		0.11350
Decreased appetite	No. of Events (%)	15 (40.5)	11 (30.6)
	Median Survival Est. (95% CI)	NC (1.71, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.358 (0.624, 2.957)
	Treatment P-value [b]		0.44856
	Interaction P-value [c]		0.70581

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Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Hyperglycaemia	No. of Events (%)	2 (5.4)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.15730
	Interaction P-value [c]		0.98776
Musculoskeletal and connective tissue disorders	No. of Events (%)	14 (37.8)	15 (41.7)
	Median Survival Est. (95% CI)	NC (3.25, NC)	NC (2.04, NC)
	Hazard Ratio (95% CI) [a]		0.860 (0.415, 1.782)
	Treatment P-value [b]		0.69280
	Interaction P-value [c]		0.55862

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Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Arthralgia	No. of Events (%)	2 (5.4)	5 (13.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.367 (0.071, 1.894)
	Treatment P-value [b]		0.21522
	Interaction P-value [c]		0.68631
Myalgia	No. of Events (%)	1 (2.7)	4 (11.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.228 (0.026, 2.043)
	Treatment P-value [b]		0.15311
	Interaction P-value [c]		0.54040

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Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Nervous system disorders	No. of Events (%)	26 (70.3)	17 (47.2)
	Median Survival Est. (95% CI)	3.06 (1.25, 4.14)	8.61 (2.27, NC)
	Hazard Ratio (95% CI) [a]		1.594 (0.865, 2.939)
	Treatment P-value [b]		0.14362
	Interaction P-value [c]		0.74954
Dysgeusia	No. of Events (%)	9 (24.3)	4 (11.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.331 (0.718, 7.570)
	Treatment P-value [b]		0.15224
	Interaction P-value [c]		0.49469

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Peripheral motor neuropathy	No. of Events (%)	1 (2.7)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.34111
	Interaction P-value [c]		0.99995
Peripheral sensory neuropathy	No. of Events (%)	15 (40.5)	8 (22.2)
	Median Survival Est. (95% CI)	NC (4.17, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.836 (0.778, 4.332)
	Treatment P-value [b]		0.18384
	Interaction P-value [c]		0.56964

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Taste disorder	No. of Events (%)	0	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		NA
	Interaction P-value [c]		0.99808
Renal and urinary disorders	No. of Events (%)	7 (18.9)	7 (19.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.003 (0.352, 2.859)
	Treatment P-value [b]		0.95263
	Interaction P-value [c]		0.46548

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Acute kidney injury	No. of Events (%)	1 (2.7)	1 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.995 (0.062, 15.903)
	Treatment P-value [b]		0.99227
	Interaction P-value [c]		0.53118
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	11 (29.7)	7 (19.4)
	Median Survival Est. (95% CI)	NC (5.85, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.591 (0.617, 4.103)
	Treatment P-value [b]		0.33037
	Interaction P-value [c]		0.90500

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table TEAE.KM.S9.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Skin and subcutaneous tissue disorders	No. of Events (%)	27 (73.0)	20 (55.6)
	Median Survival Est. (95% CI)	0.69 (0.30, 1.18)	2.10 (0.46, NC)
	Hazard Ratio (95% CI) [a]		1.583 (0.887, 2.823)
	Treatment P-value [b]		0.16232
	Interaction P-value [c]		0.26671
Drug eruption	No. of Events (%)	2 (5.4)	3 (8.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.638 (0.107, 3.816)
	Treatment P-value [b]		0.62284
	Interaction P-value [c]		0.00787

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S9.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Dry skin	No. of Events (%)	3 (8.1)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.09014
	Interaction P-value [c]		0.98411
Pruritus	No. of Events (%)	11 (29.7)	3 (8.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.359 (1.216, 15.626)
	Treatment P-value [b]		0.01654
	Interaction P-value [c]		0.59749

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S9.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Rash	No. of Events (%)	5 (13.5)	3 (8.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.677 (0.401, 7.020)
	Treatment P-value [b]		0.46960
	Interaction P-value [c]		0.38509
Rash maculo-papular	No. of Events (%)	6 (16.2)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.01194
	Interaction P-value [c]		0.98489

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Table TEAE.KM.S9.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Skin hyperpigmentation	No. of Events (%)	2 (5.4)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.15718
	Interaction P-value [c]		0.99195

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Table TEAE.KM.S10.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Any Event	No. of Events (%)	60 (98.4)	47 (95.9)
	Median Survival Est. (95% CI)	0.16 (0.10, 0.20)	0.16 (0.10, 0.20)
	Hazard Ratio (95% CI) [a]		1.086 (0.741, 1.592)
	Treatment P-value [b]		0.75776
	Interaction P-value [c]		0.40003
Blood and lymphatic system disorders	No. of Events (%)	15 (24.6)	25 (51.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	4.11 (0.82, NC)
	Hazard Ratio (95% CI) [a]		0.353 (0.186, 0.671)
	Treatment P-value [b]		0.00142
	Interaction P-value [c]		0.04661

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S10.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Anaemia	No. of Events (%)	10 (16.4)	17 (34.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (4.11, NC)
	Hazard Ratio (95% CI) [a]		0.395 (0.181, 0.862)
	Treatment P-value [b]		0.02137
	Interaction P-value [c]		0.12115
Febrile neutropenia	No. of Events (%)	0	4 (8.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.02211
	Interaction P-value [c]		0.99194

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Eye disorders	No. of Events (%)	15 (24.6)	2 (4.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.517 (1.490, 28.499)
	Treatment P-value [b]		0.00372
	Interaction P-value [c]		0.37555
Dry eye	No. of Events (%)	1 (1.6)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.36707
	Interaction P-value [c]		0.99004

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Lacrimation increased	No. of Events (%)	4 (6.6)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.07738
	Interaction P-value [c]		0.98922
Vision blurred	No. of Events (%)	1 (1.6)	2 (4.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.386 (0.035, 4.252)
	Treatment P-value [b]		0.42697
	Interaction P-value [c]		0.04417

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S10.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Diarrhoea	No. of Events (%)	16 (26.2)	11 (22.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.131 (0.525, 2.436)
	Treatment P-value [b]		0.76554
	Interaction P-value [c]		0.39993
Dry mouth	No. of Events (%)	4 (6.6)	3 (6.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.071 (0.240, 4.786)
	Treatment P-value [b]		0.93437
	Interaction P-value [c]		0.04372

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Table TEAE.KM.S10.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Chills	No. of Events (%)	1 (1.6)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.36707
	Interaction P-value [c]		0.99227
Fatigue	No. of Events (%)	21 (34.4)	19 (38.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (2.10, NC)
	Hazard Ratio (95% CI) [a]		0.817 (0.439, 1.519)
	Treatment P-value [b]		0.53820
	Interaction P-value [c]		0.08588

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Infections and infestations	No. of Events (%)	35 (57.4)	19 (38.8)
	Median Survival Est. (95% CI)	3.15 (2.20, NC)	NC (3.78, NC)
	Hazard Ratio (95% CI) [a]		1.627 (0.931, 2.845)
	Treatment P-value [b]		0.09550
	Interaction P-value [c]		0.86193
Conjunctivitis	No. of Events (%)	5 (8.2)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.04554
	Interaction P-value [c]		0.99255

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Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Alanine aminotransferase increased	No. of Events (%)	6 (9.8)	1 (2.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.006 (0.603, 41.585)
	Treatment P-value [b]		0.10234
	Interaction P-value [c]		0.81942
Aspartate aminotransferase increased	No. of Events (%)	8 (13.1)	1 (2.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.668 (0.834, 53.316)
	Treatment P-value [b]		0.03983
	Interaction P-value [c]		0.74088

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Blood creatinine increased	No. of Events (%)	1 (1.6)	1 (2.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.789 (0.049, 12.613)
	Treatment P-value [b]		0.86908
	Interaction P-value [c]		0.21395
Neutrophil count decreased	No. of Events (%)	7 (11.5)	8 (16.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.655 (0.238, 1.806)
	Treatment P-value [b]		0.38996
	Interaction P-value [c]		0.66639

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Weight decreased	No. of Events (%)	7 (11.5)	3 (6.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.873 (0.484, 7.242)
	Treatment P-value [b]		0.36872
	Interaction P-value [c]		0.58027
White blood cell count decreased	No. of Events (%)	3 (4.9)	3 (6.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.777 (0.157, 3.849)
	Treatment P-value [b]		0.76188
	Interaction P-value [c]		0.46323

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Astellas: 7465-CL-0301
Table TEAE.KM.S10.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Metabolism and nutrition disorders	No. of Events (%)	35 (57.4)	24 (49.0)
	Median Survival Est. (95% CI)	2.53 (0.62, NC)	NC (0.82, NC)
	Hazard Ratio (95% CI) [a]		1.226 (0.729, 2.061)
	Treatment P-value [b]		0.45329
	Interaction P-value [c]		0.76275
Decreased appetite	No. of Events (%)	29 (47.5)	15 (30.6)
	Median Survival Est. (95% CI)	NC (1.77, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.667 (0.893, 3.109)
	Treatment P-value [b]		0.11297
	Interaction P-value [c]		0.67360

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S10.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Hyperglycaemia	No. of Events (%)	7 (11.5)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.01560
	Interaction P-value [c]		0.98957
Musculoskeletal and connective tissue disorders	No. of Events (%)	23 (37.7)	20 (40.8)
	Median Survival Est. (95% CI)	NC (6.47, NC)	NC (2.83, NC)
	Hazard Ratio (95% CI) [a]		0.841 (0.462, 1.532)
	Treatment P-value [b]		0.54847
	Interaction P-value [c]		0.78716

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Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Arthralgia	No. of Events (%)	4 (6.6)	9 (18.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.318 (0.098, 1.033)
	Treatment P-value [b]		0.04680
	Interaction P-value [c]		0.29703
Myalgia	No. of Events (%)	3 (4.9)	4 (8.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.583 (0.131, 2.607)
	Treatment P-value [b]		0.48202
	Interaction P-value [c]		0.77040

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Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Nervous system disorders	No. of Events (%)	43 (70.5)	24 (49.0)
	Median Survival Est. (95% CI)	2.73 (1.51, 3.42)	6.97 (1.84, NC)
	Hazard Ratio (95% CI) [a]		1.590 (0.964, 2.621)
	Treatment P-value [b]		0.06150
	Interaction P-value [c]		0.72270
Dysgeusia	No. of Events (%)	16 (26.2)	5 (10.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.864 (1.049, 7.819)
	Treatment P-value [b]		0.03421
	Interaction P-value [c]		0.87231

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Table TEAE.KM.S10.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Peripheral sensory neuropathy	No. of Events (%)	23 (37.7)	9 (18.4)
	Median Survival Est. (95% CI)	NC (5.29, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.086 (0.965, 4.508)
	Treatment P-value [b]		0.05862
	Interaction P-value [c]		0.27110
Renal and urinary disorders	No. of Events (%)	14 (23.0)	9 (18.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.285 (0.556, 2.970)
	Treatment P-value [b]		0.54733
	Interaction P-value [c]		0.75449

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Table TEAE.KM.S10.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Acute kidney injury	No. of Events (%)	4 (6.6)	1 (2.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.188 (0.356, 28.517)
	Treatment P-value [b]		0.27331
	Interaction P-value [c]		0.74936
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	24 (39.3)	9 (18.4)
	Median Survival Est. (95% CI)	NC (4.83, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.296 (1.067, 4.939)
	Treatment P-value [b]		0.02618
	Interaction P-value [c]		0.39410

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Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Skin and subcutaneous tissue disorders	No. of Events (%)	52 (85.2)	24 (49.0)
	Median Survival Est. (95% CI)	0.36 (0.33, 0.53)	3.78 (0.69, NC)
	Hazard Ratio (95% CI) [a]		3.081 (1.895, 5.008)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.15353
Drug eruption	No. of Events (%)	10 (16.4)	2 (4.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.297 (0.941, 19.617)
	Treatment P-value [b]		0.04233
	Interaction P-value [c]		0.59997

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Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Dry skin	No. of Events (%)	11 (18.0)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00217
	Interaction P-value [c]		0.98699
Pruritus	No. of Events (%)	21 (34.4)	1 (2.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		20.604 (2.771, 153.188)
	Treatment P-value [b]		0.00003
	Interaction P-value [c]		0.26409

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Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Rash	No. of Events (%)	13 (21.3)	4 (8.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.888 (0.942, 8.858)
	Treatment P-value [b]		0.05422
	Interaction P-value [c]		0.85427
Rash erythematous	No. of Events (%)	0	1 (2.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.25741
	Interaction P-value [c]		0.99331

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Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Rash maculo-papular	No. of Events (%)	8 (13.1)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00964
	Interaction P-value [c]		0.98348
Skin hyperpigmentation	No. of Events (%)	3 (4.9)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.12105
	Interaction P-value [c]		0.99995

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Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Any Event	No. of Events (%)	197 (97.5)	201 (99.5)
	Median Survival Est. (95% CI)	0.18 (0.16, 0.23)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.903 (0.741, 1.100)
	Treatment P-value [b]		0.28044
	Interaction P-value [c]		0.40003
Blood and lymphatic system disorders	No. of Events (%)	62 (30.7)	76 (37.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (12.94, NC)
	Hazard Ratio (95% CI) [a]		0.736 (0.526, 1.030)
	Treatment P-value [b]		0.06704
	Interaction P-value [c]		0.04661

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Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Anaemia	No. of Events (%)	44 (21.8)	53 (26.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.790 (0.530, 1.178)
	Treatment P-value [b]		0.23199
	Interaction P-value [c]		0.12115
Febrile neutropenia	No. of Events (%)	3 (1.5)	10 (5.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.288 (0.079, 1.048)
	Treatment P-value [b]		0.04430
	Interaction P-value [c]		0.99194

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Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Eye disorders	No. of Events (%)	58 (28.7)	20 (9.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.219 (1.936, 5.351)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.37555
Dry eye	No. of Events (%)	16 (7.9)	3 (1.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.336 (1.555, 18.317)
	Treatment P-value [b]		0.00289
	Interaction P-value [c]		0.99004

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Table TEAE.KM.S10.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Lacrimation increased	No. of Events (%)	22 (10.9)	9 (4.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.485 (1.144, 5.398)
	Treatment P-value [b]		0.01662
	Interaction P-value [c]		0.98922
Vision blurred	No. of Events (%)	14 (6.9)	2 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.982 (1.587, 30.713)
	Treatment P-value [b]		0.00279
	Interaction P-value [c]		0.04417

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
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Astellas: 7465-CL-0301
Table TEAE.KM.S10.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Diarrhoea	No. of Events (%)	70 (34.7)	45 (22.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.632 (1.122, 2.374)
	Treatment P-value [b]		0.00927
	Interaction P-value [c]		0.39993
Dry mouth	No. of Events (%)	18 (8.9)	2 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.216 (2.138, 39.719)
	Treatment P-value [b]		0.00029
	Interaction P-value [c]		0.04372

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table TEAE.KM.S10.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Chills	No. of Events (%)	15 (7.4)	6 (3.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.525 (0.980, 6.509)
	Treatment P-value [b]		0.04726
	Interaction P-value [c]		0.99227
Fatigue	No. of Events (%)	76 (37.6)	51 (25.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.528 (1.072, 2.179)
	Treatment P-value [b]		0.01746
	Interaction P-value [c]		0.08588

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Table TEAE.KM.S10.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Infections and infestations	No. of Events (%)	105 (52.0)	74 (36.6)
	Median Survival Est. (95% CI)	5.45 (3.25, NC)	NC (10.41, NC)
	Hazard Ratio (95% CI) [a]		1.538 (1.142, 2.072)
	Treatment P-value [b]		0.00451
	Interaction P-value [c]		0.86193
Conjunctivitis	No. of Events (%)	13 (6.4)	2 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.522 (1.472, 28.903)
	Treatment P-value [b]		0.00458
	Interaction P-value [c]		0.99255

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Table TEAE.KM.S10.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Alanine aminotransferase increased	No. of Events (%)	15 (7.4)	4 (2.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.791 (1.258, 11.424)
	Treatment P-value [b]		0.01094
	Interaction P-value [c]		0.81942
Aspartate aminotransferase increased	No. of Events (%)	20 (9.9)	2 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		10.230 (2.391, 43.766)
	Treatment P-value [b]		0.00010
	Interaction P-value [c]		0.74088

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The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Blood creatinine increased	No. of Events (%)	20 (9.9)	4 (2.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.195 (1.776, 15.200)
	Treatment P-value [b]		0.00079
	Interaction P-value [c]		0.21395
Neutrophil count decreased	No. of Events (%)	21 (10.4)	37 (18.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.509 (0.298, 0.869)
	Treatment P-value [b]		0.01286
	Interaction P-value [c]		0.66639

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Weight decreased	No. of Events (%)	38 (18.8)	14 (6.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.847 (1.543, 5.255)
	Treatment P-value [b]		0.00045
	Interaction P-value [c]		0.58027
White blood cell count decreased	No. of Events (%)	11 (5.4)	25 (12.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.403 (0.198, 0.820)
	Treatment P-value [b]		0.01026
	Interaction P-value [c]		0.46323

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Metabolism and nutrition disorders	No. of Events (%)	118 (58.4)	90 (44.6)
	Median Survival Est. (95% CI)	2.20 (1.71, 5.39)	NC (5.29, NC)
	Hazard Ratio (95% CI) [a]		1.342 (1.020, 1.766)
	Treatment P-value [b]		0.03375
	Interaction P-value [c]		0.76275
Decreased appetite	No. of Events (%)	82 (40.6)	57 (28.2)
	Median Survival Est. (95% CI)	NC (9.10, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.431 (1.020, 2.007)
	Treatment P-value [b]		0.03639
	Interaction P-value [c]		0.67360

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Table TEAE.KM.S10.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Hyperglycaemia	No. of Events (%)	20 (9.9)	6 (3.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.426 (1.376, 8.531)
	Treatment P-value [b]		0.00500
	Interaction P-value [c]		0.98957
Musculoskeletal and connective tissue disorders	No. of Events (%)	69 (34.2)	79 (39.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.766 (0.555, 1.058)
	Treatment P-value [b]		0.11392
	Interaction P-value [c]		0.78716

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Arthralgia	No. of Events (%)	16 (7.9)	23 (11.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.649 (0.343, 1.229)
	Treatment P-value [b]		0.18482
	Interaction P-value [c]		0.29703
Myalgia	No. of Events (%)	10 (5.0)	21 (10.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.455 (0.214, 0.965)
	Treatment P-value [b]		0.03685
	Interaction P-value [c]		0.77040

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Nervous system disorders	No. of Events (%)	126 (62.4)	94 (46.5)
	Median Survival Est. (95% CI)	2.83 (2.07, 3.81)	8.61 (3.48, NC)
	Hazard Ratio (95% CI) [a]		1.435 (1.098, 1.875)
	Treatment P-value [b]		0.00794
	Interaction P-value [c]		0.72270
Dysgeusia	No. of Events (%)	50 (24.8)	17 (8.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.146 (1.814, 5.455)
	Treatment P-value [b]		0.00002
	Interaction P-value [c]		0.87231

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Peripheral sensory neuropathy	No. of Events (%)	66 (32.7)	48 (23.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.290 (0.889, 1.871)
	Treatment P-value [b]		0.17876
	Interaction P-value [c]		0.27110
Renal and urinary disorders	No. of Events (%)	54 (26.7)	37 (18.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.492 (0.982, 2.267)
	Treatment P-value [b]		0.05909
	Interaction P-value [c]		0.75449

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Acute kidney injury	No. of Events (%)	13 (6.4)	6 (3.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.157 (0.820, 5.677)
	Treatment P-value [b]		0.11417
	Interaction P-value [c]		0.74936
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	69 (34.2)	46 (22.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.585 (1.091, 2.302)
	Treatment P-value [b]		0.01495
	Interaction P-value [c]		0.39410

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Skin and subcutaneous tissue disorders	No. of Events (%)	158 (78.2)	103 (51.0)
	Median Survival Est. (95% CI)	0.69 (0.49, 0.89)	3.25 (1.45, NC)
	Hazard Ratio (95% CI) [a]		2.073 (1.615, 2.660)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.15353
Drug eruption	No. of Events (%)	15 (7.4)	2 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.572 (1.732, 33.105)
	Treatment P-value [b]		0.00159
	Interaction P-value [c]		0.59997

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table TEAE.KM.S10.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Dry skin	No. of Events (%)	36 (17.8)	8 (4.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.832 (2.246, 10.397)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.98699
Pruritus	No. of Events (%)	73 (36.1)	14 (6.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.277 (3.542, 11.123)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.26409

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table TEAE.KM.S10.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Rash	No. of Events (%)	34 (16.8)	11 (5.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.265 (1.654, 6.445)
	Treatment P-value [b]		0.00032
	Interaction P-value [c]		0.85427
Rash erythematous	No. of Events (%)	10 (5.0)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00158
	Interaction P-value [c]		0.99331

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table TEAE.KM.S10.SAF: Time to First Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Rash maculo-papular	No. of Events (%)	39 (19.3)	4 (2.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		10.736 (3.836, 30.046)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.98348
Skin hyperpigmentation	No. of Events (%)	12 (5.9)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00045
	Interaction P-value [c]		0.99995

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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4.3 Subgruppenanalysen zu den progressionsbereinigten unerwünschten Ereignissen

Astellas: 7465-CL-0301
Table TEAE.wDP.KM.S1.SAF: Time to First Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: <65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Any Event	No. of Events (%)	105 (99.1)	101 (98.1)
	Median Survival Est. (95% CI)	0.16 (0.13, 0.23)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.987 (0.751, 1.298)
	Treatment P-value [b]		0.99496
	Interaction P-value [c]		0.55172

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table TEAE.wDP.KM.S1.SAF: Time to First Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Any Event	No. of Events (%)	184 (96.8)	186 (98.9)
	Median Survival Est. (95% CI)	0.23 (0.16, 0.26)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.890 (0.726, 1.092)
	Treatment P-value [b]		0.23363
	Interaction P-value [c]		0.55172

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50

Astellas: 7465-CL-0301
Table TEAE.wDP.KM.S2.SAF: Time to First Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Any Event	No. of Events (%)	240 (98.0)	223 (98.7)
	Median Survival Est. (95% CI)	0.20 (0.16, 0.23)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.927 (0.772, 1.113)
	Treatment P-value [b]		0.41647
	Interaction P-value [c]		0.92328

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table TEAE.wDP.KM.S2.SAF: Time to First Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Any Event	No. of Events (%)	49 (96.1)	64 (98.5)
	Median Survival Est. (95% CI)	0.20 (0.13, 0.26)	0.13 (0.07, 0.23)
	Hazard Ratio (95% CI) [a]		0.909 (0.626, 1.319)
	Treatment P-value [b]		0.64849
	Interaction P-value [c]		0.92328

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table TEAE.wDP.KM.S3.SAF: Time to First Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Any Event	No. of Events (%)	230 (98.3)	215 (98.2)
	Median Survival Est. (95% CI)	0.20 (0.16, 0.23)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		1.004 (0.832, 1.211)
	Treatment P-value [b]		0.90002
	Interaction P-value [c]		0.06909

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table TEAE.wDP.KM.S3.SAF: Time to First Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Any Event	No. of Events (%)	59 (95.2)	72 (100.0)
	Median Survival Est. (95% CI)	0.20 (0.13, 0.26)	0.13 (0.10, 0.20)
	Hazard Ratio (95% CI) [a]		0.696 (0.492, 0.984)
	Treatment P-value [b]		0.05040
	Interaction P-value [c]		0.06909

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table TEAE.wDP.KM.S4.SAF: Time to First Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Region, Level: Western Europe

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Any Event	No. of Events (%)	117 (95.9)	120 (97.6)
	Median Survival Est. (95% CI)	0.23 (0.16, 0.26)	0.13 (0.07, 0.16)
	Hazard Ratio (95% CI) [a]		0.868 (0.673, 1.121)
	Treatment P-value [b]		0.37921
	Interaction P-value [c]		0.72429

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table TEAE.wDP.KM.S4.SAF: Time to First Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Region, Level: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Any Event	No. of Events (%)	41 (97.6)	39 (100.0)
	Median Survival Est. (95% CI)	0.26 (0.13, 0.26)	0.10 (0.07, 0.20)
	Hazard Ratio (95% CI) [a]		0.873 (0.562, 1.354)
	Treatment P-value [b]		0.39603
	Interaction P-value [c]		0.72429

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table TEAE.wDP.KM.S4.SAF: Time to First Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Region, Level: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Any Event	No. of Events (%)	131 (99.2)	128 (99.2)
	Median Survival Est. (95% CI)	0.16 (0.13, 0.23)	0.16 (0.13, 0.16)
	Hazard Ratio (95% CI) [a]		0.995 (0.780, 1.270)
	Treatment P-value [b]		0.94129
	Interaction P-value [c]		0.72429

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table TEAE.wDP.KM.S5.SAF: Time to First Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Any Event	No. of Events (%)	117 (97.5)	117 (98.3)
	Median Survival Est. (95% CI)	0.20 (0.13, 0.26)	0.13 (0.10, 0.20)
	Hazard Ratio (95% CI) [a]		1.010 (0.781, 1.305)
	Treatment P-value [b]		0.90125
	Interaction P-value [c]		0.35773

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table TEAE.wDP.KM.S5.SAF: Time to First Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Any Event	No. of Events (%)	172 (97.7)	170 (98.8)
	Median Survival Est. (95% CI)	0.20 (0.16, 0.23)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.864 (0.698, 1.068)
	Treatment P-value [b]		0.17185
	Interaction P-value [c]		0.35773

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table TEAE.wDP.KM.S6.SAF: Time to First Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Any Event	No. of Events (%)	89 (96.7)	83 (95.4)
	Median Survival Est. (95% CI)	0.16 (0.13, 0.23)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		1.089 (0.806, 1.470)
	Treatment P-value [b]		0.75866
	Interaction P-value [c]		0.19272

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table TEAE.wDP.KM.S6.SAF: Time to First Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Any Event	No. of Events (%)	200 (98.0)	204 (100.0)
	Median Survival Est. (95% CI)	0.23 (0.16, 0.26)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.858 (0.706, 1.044)
	Treatment P-value [b]		0.13328
	Interaction P-value [c]		0.19272

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table TEAE.wDP.KM.S7.SAF: Time to First Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Any Event	No. of Events (%)	137 (97.9)	105 (98.1)
	Median Survival Est. (95% CI)	0.16 (0.13, 0.23)	0.16 (0.10, 0.26)
	Hazard Ratio (95% CI) [a]		1.183 (0.916, 1.528)
	Treatment P-value [b]		0.20495
	Interaction P-value [c]		0.03544

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table TEAE.wDP.KM.S7.SAF: Time to First Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Any Event	No. of Events (%)	84 (98.8)	108 (99.1)
	Median Survival Est. (95% CI)	0.26 (0.16, 0.26)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.824 (0.619, 1.097)
	Treatment P-value [b]		0.11848
	Interaction P-value [c]		0.03544

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table TEAE.wDP.KM.S7.SAF: Time to First Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Any Event	No. of Events (%)	68 (95.8)	74 (98.7)
	Median Survival Est. (95% CI)	0.20 (0.13, 0.26)	0.07 (0.07, 0.13)
	Hazard Ratio (95% CI) [a]		0.709 (0.510, 0.986)
	Treatment P-value [b]		0.05617
	Interaction P-value [c]		0.03544

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50

Astellas: 7465-CL-0301
Table TEAE.wDP.KM.S8.SAF: Time to First Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Any Event	No. of Events (%)	95 (99.0)	100 (98.0)
	Median Survival Est. (95% CI)	0.23 (0.16, 0.26)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.844 (0.637, 1.119)
	Treatment P-value [b]		0.20688
	Interaction P-value [c]		0.44642

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50

Astellas: 7465-CL-0301
Table TEAE.wDP.KM.S8.SAF: Time to First Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Any Event	No. of Events (%)	194 (97.0)	187 (98.9)
	Median Survival Est. (95% CI)	0.16 (0.13, 0.23)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.966 (0.789, 1.181)
	Treatment P-value [b]		0.78801
	Interaction P-value [c]		0.44642

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50

Astellas: 7465-CL-0301
Table TEAE.wDP.KM.S9.SAF: Time to First Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Any Event	No. of Events (%)	253 (97.7)	251 (98.4)
	Median Survival Est. (95% CI)	0.20 (0.16, 0.23)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.945 (0.793, 1.126)
	Treatment P-value [b]		0.56704
	Interaction P-value [c]		0.44213

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table TEAE.wDP.KM.S9.SAF: Time to First Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Any Event	No. of Events (%)	36 (97.3)	36 (100.0)
	Median Survival Est. (95% CI)	0.23 (0.13, 0.26)	0.13 (0.10, 0.20)
	Hazard Ratio (95% CI) [a]		0.778 (0.490, 1.236)
	Treatment P-value [b]		0.13319
	Interaction P-value [c]		0.44213

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50

Astellas: 7465-CL-0301
Table TEAE.wDP.KM.S10.SAF: Time to First Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Any Event	No. of Events (%)	60 (98.4)	47 (95.9)
	Median Survival Est. (95% CI)	0.16 (0.10, 0.23)	0.16 (0.10, 0.20)
	Hazard Ratio (95% CI) [a]		1.080 (0.736, 1.583)
	Treatment P-value [b]		0.75429
	Interaction P-value [c]		0.44161

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table TEAE.wDP.KM.S10.SAF: Time to First Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Any Event	No. of Events (%)	196 (97.0)	200 (99.0)
	Median Survival Est. (95% CI)	0.18 (0.16, 0.23)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.912 (0.748, 1.111)
	Treatment P-value [b]		0.32107
	Interaction P-value [c]		0.44161

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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4.4 Subgruppenanalysen zu den nicht schweren (CTCAE Grad < 3) unerwünschten Ereignissen

4.4.1 Primäranalyse

Astellas: 7465-CL-0301
Table AENSV.KM.S1.SAF: Time to First Not Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: <65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Any Event	No. of Events (%)	105 (99.1)	101 (98.1)
	Median Survival Est. (95% CI)	0.16 (0.13, 0.23)	0.13 (0.13, 0.20)
	Hazard Ratio (95% CI) [a]		1.027 (0.781, 1.350)
	Treatment P-value [b]		0.84325
	Interaction P-value [c]		0.75589

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table AENSV.KM.S1.SAF: Time to First Not Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Any Event	No. of Events (%)	184 (96.8)	182 (96.8)
	Median Survival Est. (95% CI)	0.23 (0.16, 0.26)	0.15 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.973 (0.792, 1.195)
	Treatment P-value [b]		0.80486
	Interaction P-value [c]		0.75589

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
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Astellas: 7465-CL-0301
Table AENSV.KM.S2.SAF: Time to First Not Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Any Event	No. of Events (%)	240 (98.0)	219 (96.9)
	Median Survival Est. (95% CI)	0.20 (0.16, 0.26)	0.13 (0.13, 0.16)
	Hazard Ratio (95% CI) [a]		1.004 (0.836, 1.207)
	Treatment P-value [b]		0.93457
	Interaction P-value [c]		0.77942

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.KM.S2.SAF: Time to First Not Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Any Event	No. of Events (%)	49 (96.1)	64 (98.5)
	Median Survival Est. (95% CI)	0.20 (0.13, 0.26)	0.13 (0.07, 0.23)
	Hazard Ratio (95% CI) [a]		0.947 (0.652, 1.374)
	Treatment P-value [b]		0.83467
	Interaction P-value [c]		0.77942

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
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Astellas: 7465-CL-0301
Table AENSV.KM.S3.SAF: Time to First Not Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Any Event	No. of Events (%)	230 (98.3)	211 (96.3)
	Median Survival Est. (95% CI)	0.20 (0.16, 0.26)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		1.079 (0.894, 1.302)
	Treatment P-value [b]		0.35077
	Interaction P-value [c]		0.06737

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.KM.S3.SAF: Time to First Not Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Any Event	No. of Events (%)	59 (95.2)	72 (100.0)
	Median Survival Est. (95% CI)	0.20 (0.13, 0.26)	0.13 (0.10, 0.20)
	Hazard Ratio (95% CI) [a]		0.747 (0.528, 1.055)
	Treatment P-value [b]		0.14013
	Interaction P-value [c]		0.06737

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.KM.S4.SAF: Time to First Not Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Western Europe

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Any Event	No. of Events (%)	117 (95.9)	116 (94.3)
	Median Survival Est. (95% CI)	0.23 (0.16, 0.26)	0.13 (0.07, 0.20)
	Hazard Ratio (95% CI) [a]		0.972 (0.751, 1.257)
	Treatment P-value [b]		0.96854
	Interaction P-value [c]		0.83479

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.KM.S4.SAF: Time to First Not Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Any Event	No. of Events (%)	41 (97.6)	39 (100.0)
	Median Survival Est. (95% CI)	0.26 (0.13, 0.26)	0.13 (0.07, 0.23)
	Hazard Ratio (95% CI) [a]		0.898 (0.579, 1.394)
	Treatment P-value [b]		0.58005
	Interaction P-value [c]		0.83479

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.KM.S4.SAF: Time to First Not Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Any Event	No. of Events (%)	131 (99.2)	128 (99.2)
	Median Survival Est. (95% CI)	0.16 (0.13, 0.23)	0.16 (0.13, 0.20)
	Hazard Ratio (95% CI) [a]		1.039 (0.814, 1.326)
	Treatment P-value [b]		0.70293
	Interaction P-value [c]		0.83479

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.KM.S5.SAF: Time to First Not Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Any Event	No. of Events (%)	117 (97.5)	117 (98.3)
	Median Survival Est. (95% CI)	0.20 (0.13, 0.26)	0.16 (0.10, 0.23)
	Hazard Ratio (95% CI) [a]		1.060 (0.820, 1.370)
	Treatment P-value [b]		0.64119
	Interaction P-value [c]		0.48447

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.KM.S5.SAF: Time to First Not Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Any Event	No. of Events (%)	172 (97.7)	166 (96.5)
	Median Survival Est. (95% CI)	0.20 (0.16, 0.26)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.941 (0.760, 1.165)
	Treatment P-value [b]		0.60922
	Interaction P-value [c]		0.48447

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.KM.S6.SAF: Time to First Not Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Any Event	No. of Events (%)	89 (96.7)	83 (95.4)
	Median Survival Est. (95% CI)	0.16 (0.13, 0.23)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		1.061 (0.786, 1.433)
	Treatment P-value [b]		0.84414
	Interaction P-value [c]		0.59231

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.KM.S6.SAF: Time to First Not Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Any Event	No. of Events (%)	200 (98.0)	200 (98.0)
	Median Survival Est. (95% CI)	0.23 (0.16, 0.26)	0.16 (0.13, 0.20)
	Hazard Ratio (95% CI) [a]		0.963 (0.791, 1.172)
	Treatment P-value [b]		0.79030
	Interaction P-value [c]		0.59231

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.KM.S7.SAF: Time to First Not Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Any Event	No. of Events (%)	137 (97.9)	104 (97.2)
	Median Survival Est. (95% CI)	0.18 (0.13, 0.23)	0.16 (0.10, 0.26)
	Hazard Ratio (95% CI) [a]		1.188 (0.920, 1.535)
	Treatment P-value [b]		0.16650
	Interaction P-value [c]		0.18443

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.KM.S7.SAF: Time to First Not Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Any Event	No. of Events (%)	84 (98.8)	107 (98.2)
	Median Survival Est. (95% CI)	0.26 (0.16, 0.26)	0.13 (0.13, 0.16)
	Hazard Ratio (95% CI) [a]		0.906 (0.680, 1.206)
	Treatment P-value [b]		0.44570
	Interaction P-value [c]		0.18443

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.KM.S7.SAF: Time to First Not Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Any Event	No. of Events (%)	68 (95.8)	72 (96.0)
	Median Survival Est. (95% CI)	0.20 (0.13, 0.26)	0.10 (0.07, 0.16)
	Hazard Ratio (95% CI) [a]		0.832 (0.597, 1.160)
	Treatment P-value [b]		0.31002
	Interaction P-value [c]		0.18443

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.KM.S8.SAF: Time to First Not Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Any Event	No. of Events (%)	95 (99.0)	98 (96.1)
	Median Survival Est. (95% CI)	0.21 (0.16, 0.26)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.892 (0.672, 1.183)
	Treatment P-value [b]		0.43987
	Interaction P-value [c]		0.36597

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.KM.S8.SAF: Time to First Not Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Any Event	No. of Events (%)	194 (97.0)	185 (97.9)
	Median Survival Est. (95% CI)	0.20 (0.13, 0.26)	0.16 (0.13, 0.20)
	Hazard Ratio (95% CI) [a]		1.046 (0.855, 1.281)
	Treatment P-value [b]		0.56471
	Interaction P-value [c]		0.36597

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.KM.S9.SAF: Time to First Not Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Any Event	No. of Events (%)	253 (97.7)	247 (96.9)
	Median Survival Est. (95% CI)	0.20 (0.16, 0.26)	0.13 (0.13, 0.16)
	Hazard Ratio (95% CI) [a]		1.013 (0.849, 1.207)
	Treatment P-value [b]		0.81667
	Interaction P-value [c]		0.49072

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.KM.S9.SAF: Time to First Not Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Any Event	No. of Events (%)	36 (97.3)	36 (100.0)
	Median Survival Est. (95% CI)	0.23 (0.13, 0.26)	0.13 (0.10, 0.23)
	Hazard Ratio (95% CI) [a]		0.851 (0.536, 1.351)
	Treatment P-value [b]		0.32864
	Interaction P-value [c]		0.49072

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.KM.S10.SAF: Time to First Not Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Any Event	No. of Events (%)	60 (98.4)	46 (93.9)
	Median Survival Est. (95% CI)	0.16 (0.10, 0.20)	0.16 (0.10, 0.20)
	Hazard Ratio (95% CI) [a]		1.083 (0.737, 1.590)
	Treatment P-value [b]		0.73715
	Interaction P-value [c]		0.72453

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.KM.S10.SAF: Time to First Not Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Any Event	No. of Events (%)	196 (97.0)	198 (98.0)
	Median Survival Est. (95% CI)	0.20 (0.16, 0.26)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		1.001 (0.821, 1.221)
	Treatment P-value [b]		0.95757
	Interaction P-value [c]		0.72453

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

4.4.2 Progressionsbereinigte Auswertungen

Astellas: 7465-CL-0301
Table AENSV.wDP.KM.S1.SAF: Time to First Not Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: <65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Any Event	No. of Events (%)	105 (99.1)	101 (98.1)
	Median Survival Est. (95% CI)	0.16 (0.13, 0.23)	0.13 (0.13, 0.20)
	Hazard Ratio (95% CI) [a]		1.021 (0.777, 1.342)
	Treatment P-value [b]		0.86711
	Interaction P-value [c]		0.76320

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

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Table AENSV.wDP.KM.S1.SAF: Time to First Not Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Any Event	No. of Events (%)	184 (96.8)	182 (96.8)
	Median Survival Est. (95% CI)	0.23 (0.16, 0.26)	0.15 (0.10, 0.20)
	Hazard Ratio (95% CI) [a]		0.969 (0.789, 1.190)
	Treatment P-value [b]		0.77644
	Interaction P-value [c]		0.76320

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

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Table AENSV.wDP.KM.S2.SAF: Time to First Not Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Any Event	No. of Events (%)	240 (98.0)	219 (96.9)
	Median Survival Est. (95% CI)	0.20 (0.16, 0.26)	0.13 (0.13, 0.16)
	Hazard Ratio (95% CI) [a]		0.998 (0.830, 1.199)
	Treatment P-value [b]		0.99503
	Interaction P-value [c]		0.82076

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.wDP.KM.S2.SAF: Time to First Not Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Any Event	No. of Events (%)	49 (96.1)	64 (98.5)
	Median Survival Est. (95% CI)	0.20 (0.13, 0.26)	0.13 (0.07, 0.23)
	Hazard Ratio (95% CI) [a]		0.951 (0.655, 1.380)
	Treatment P-value [b]		0.84224
	Interaction P-value [c]		0.82076

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.wDP.KM.S3.SAF: Time to First Not Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Any Event	No. of Events (%)	230 (98.3)	211 (96.3)
	Median Survival Est. (95% CI)	0.20 (0.16, 0.26)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		1.079 (0.894, 1.303)
	Treatment P-value [b]		0.35755
	Interaction P-value [c]		0.05226

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.wDP.KM.S3.SAF: Time to First Not Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Any Event	No. of Events (%)	59 (95.2)	72 (100.0)
	Median Survival Est. (95% CI)	0.20 (0.13, 0.26)	0.13 (0.10, 0.20)
	Hazard Ratio (95% CI) [a]		0.730 (0.517, 1.032)
	Treatment P-value [b]		0.10702
	Interaction P-value [c]		0.05226

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

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Table AENSV.wDP.KM.S4.SAF: Time to First Not Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Region, Level: Western Europe

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Any Event	No. of Events (%)	117 (95.9)	116 (94.3)
	Median Survival Est. (95% CI)	0.23 (0.16, 0.26)	0.13 (0.07, 0.20)
	Hazard Ratio (95% CI) [a]		0.961 (0.743, 1.243)
	Treatment P-value [b]		0.94226
	Interaction P-value [c]		0.83122

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.wDP.KM.S4.SAF: Time to First Not Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Region, Level: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Any Event	No. of Events (%)	41 (97.6)	39 (100.0)
	Median Survival Est. (95% CI)	0.26 (0.13, 0.26)	0.13 (0.07, 0.23)
	Hazard Ratio (95% CI) [a]		0.901 (0.581, 1.398)
	Treatment P-value [b]		0.58005
	Interaction P-value [c]		0.83122

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.wDP.KM.S4.SAF: Time to First Not Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Region, Level: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Any Event	No. of Events (%)	131 (99.2)	128 (99.2)
	Median Survival Est. (95% CI)	0.16 (0.13, 0.23)	0.16 (0.13, 0.20)
	Hazard Ratio (95% CI) [a]		1.038 (0.813, 1.325)
	Treatment P-value [b]		0.70899
	Interaction P-value [c]		0.83122

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.wDP.KM.S5.SAF: Time to First Not Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Any Event	No. of Events (%)	117 (97.5)	117 (98.3)
	Median Survival Est. (95% CI)	0.20 (0.13, 0.26)	0.16 (0.10, 0.23)
	Hazard Ratio (95% CI) [a]		1.053 (0.814, 1.361)
	Treatment P-value [b]		0.66911
	Interaction P-value [c]		0.49618

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.wDP.KM.S5.SAF: Time to First Not Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Any Event	No. of Events (%)	172 (97.7)	166 (96.5)
	Median Survival Est. (95% CI)	0.20 (0.16, 0.26)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.938 (0.757, 1.161)
	Treatment P-value [b]		0.58173
	Interaction P-value [c]		0.49618

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.wDP.KM.S6.SAF: Time to First Not Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Any Event	No. of Events (%)	89 (96.7)	83 (95.4)
	Median Survival Est. (95% CI)	0.16 (0.13, 0.23)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		1.064 (0.788, 1.436)
	Treatment P-value [b]		0.84414
	Interaction P-value [c]		0.55662

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.wDP.KM.S6.SAF: Time to First Not Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Any Event	No. of Events (%)	200 (98.0)	200 (98.0)
	Median Survival Est. (95% CI)	0.23 (0.16, 0.26)	0.16 (0.13, 0.20)
	Hazard Ratio (95% CI) [a]		0.955 (0.785, 1.163)
	Treatment P-value [b]		0.72150
	Interaction P-value [c]		0.55662

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.wDP.KM.S7.SAF: Time to First Not Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Any Event	No. of Events (%)	137 (97.9)	104 (97.2)
	Median Survival Est. (95% CI)	0.18 (0.13, 0.26)	0.16 (0.10, 0.26)
	Hazard Ratio (95% CI) [a]		1.172 (0.907, 1.513)
	Treatment P-value [b]		0.20676
	Interaction P-value [c]		0.21662

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.wDP.KM.S7.SAF: Time to First Not Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Any Event	No. of Events (%)	84 (98.8)	107 (98.2)
	Median Survival Est. (95% CI)	0.26 (0.16, 0.26)	0.13 (0.13, 0.20)
	Hazard Ratio (95% CI) [a]		0.912 (0.685, 1.215)
	Treatment P-value [b]		0.47732
	Interaction P-value [c]		0.21662

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.wDP.KM.S7.SAF: Time to First Not Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Any Event	No. of Events (%)	68 (95.8)	72 (96.0)
	Median Survival Est. (95% CI)	0.20 (0.13, 0.26)	0.10 (0.07, 0.16)
	Hazard Ratio (95% CI) [a]		0.831 (0.596, 1.157)
	Treatment P-value [b]		0.31238
	Interaction P-value [c]		0.21662

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.wDP.KM.S8.SAF: Time to First Not Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Any Event	No. of Events (%)	95 (99.0)	98 (96.1)
	Median Survival Est. (95% CI)	0.23 (0.16, 0.26)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.891 (0.672, 1.182)
	Treatment P-value [b]		0.44119
	Interaction P-value [c]		0.38383

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AENSV.wDP.KM.S8.SAF: Time to First Not Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Any Event	No. of Events (%)	194 (97.0)	185 (97.9)
	Median Survival Est. (95% CI)	0.20 (0.16, 0.26)	0.16 (0.13, 0.20)
	Hazard Ratio (95% CI) [a]		1.040 (0.849, 1.273)
	Treatment P-value [b]		0.62945
	Interaction P-value [c]		0.38383

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.wDP.KM.S9.SAF: Time to First Not Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Any Event	No. of Events (%)	253 (97.7)	247 (96.9)
	Median Survival Est. (95% CI)	0.20 (0.16, 0.26)	0.13 (0.13, 0.16)
	Hazard Ratio (95% CI) [a]		1.007 (0.844, 1.201)
	Treatment P-value [b]		0.86575
	Interaction P-value [c]		0.50695

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.wDP.KM.S9.SAF: Time to First Not Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Any Event	No. of Events (%)	36 (97.3)	36 (100.0)
	Median Survival Est. (95% CI)	0.23 (0.13, 0.26)	0.13 (0.10, 0.23)
	Hazard Ratio (95% CI) [a]		0.852 (0.536, 1.353)
	Treatment P-value [b]		0.32864
	Interaction P-value [c]		0.50695

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.wDP.KM.S10.SAF: Time to First Not Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Any Event	No. of Events (%)	60 (98.4)	46 (93.9)
	Median Survival Est. (95% CI)	0.16 (0.10, 0.23)	0.16 (0.10, 0.23)
	Hazard Ratio (95% CI) [a]		1.077 (0.733, 1.583)
	Treatment P-value [b]		0.74011
	Interaction P-value [c]		0.72591

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AENSV.wDP.KM.S10.SAF: Time to First Not Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Any Event	No. of Events (%)	196 (97.0)	198 (98.0)
	Median Survival Est. (95% CI)	0.20 (0.16, 0.26)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.997 (0.818, 1.216)
	Treatment P-value [b]		0.98881
	Interaction P-value [c]		0.72591

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
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4.5 Schwere (CTCAE Grad ≥ 3) unerwünschte Ereignisse inkl. SOC und PT – Hauptebene und Subgruppenanalysen

Astellas: 7465-CL-0301
Table AESV.KM.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Any Event	No. of Events (%)	211 (71.3)	194 (66.7)
	Median Survival Est. (95% CI)	1.77 (1.28, 2.27)	1.45 (0.95, 2.17)
	Hazard Ratio (95% CI) [a]		0.976 (0.801, 1.188)
	Treatment P-value [b]		0.82523
	Homogeneity P-value [c]		NA
Blood and lymphatic system disorders	No. of Events (%)	32 (10.8)	70 (24.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.388 (0.255, 0.591)
	Treatment P-value [b]		<.00001
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESV.KM.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Anaemia	No. of Events (%)	19 (6.4)	35 (12.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.487 (0.278, 0.856)
	Treatment P-value [b]		0.01064
	Homogeneity P-value [c]		NA
Febrile neutropenia	No. of Events (%)	4 (1.4)	16 (5.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.234 (0.078, 0.700)
	Treatment P-value [b]		0.00464
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESV.KM.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Neutropenia	No. of Events (%)	14 (4.7)	22 (7.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.595 (0.304, 1.165)
	Treatment P-value [b]		0.12597
	Homogeneity P-value [c]		NA
Gastrointestinal disorders	No. of Events (%)	27 (9.1)	34 (11.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.749 (0.452, 1.243)
	Treatment P-value [b]		0.26271
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESV.KM.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Abdominal pain	No. of Events (%)	3 (1.0)	7 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.410 (0.106, 1.591)
	Treatment P-value [b]		0.18283
	Homogeneity P-value [c]		NA
Constipation	No. of Events (%)	4 (1.4)	6 (2.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.654 (0.184, 2.321)
	Treatment P-value [b]		0.50796
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

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Table AESV.KM.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Diarrhoea	No. of Events (%)	11 (3.7)	5 (1.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.130 (0.739, 6.139)
	Treatment P-value [b]		0.15145
	Homogeneity P-value [c]		NA
General disorders and administration site conditions	No. of Events (%)	41 (13.9)	31 (10.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.247 (0.781, 1.990)
	Treatment P-value [b]		0.35238
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

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Table AESV.KM.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Asthenia	No. of Events (%)	7 (2.4)	7 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.942 (0.330, 2.687)
	Treatment P-value [b]		0.91105
	Homogeneity P-value [c]		NA
Fatigue	No. of Events (%)	20 (6.8)	14 (4.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.365 (0.689, 2.706)
	Treatment P-value [b]		0.37072
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

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Table AESV.KM.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
General physical health deterioration	No. of Events (%)	3 (1.0)	7 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.407 (0.105, 1.576)
	Treatment P-value [b]		0.17858
	Homogeneity P-value [c]		NA
Infections and infestations	No. of Events (%)	52 (17.6)	33 (11.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.568 (1.013, 2.428)
	Treatment P-value [b]		0.04146
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESV.KM.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Pneumonia	No. of Events (%)	13 (4.4)	6 (2.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.092 (0.794, 5.513)
	Treatment P-value [b]		0.12649
	Homogeneity P-value [c]		NA
Urinary tract infection	No. of Events (%)	6 (2.0)	6 (2.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.942 (0.303, 2.926)
	Treatment P-value [b]		0.91824
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

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Table AESV.KM.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Urinary tract infection bacterial	No. of Events (%)	9 (3.0)	4 (1.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.202 (0.677, 7.160)
	Treatment P-value [b]		0.17820
	Homogeneity P-value [c]		NA
Investigations	No. of Events (%)	46 (15.5)	59 (20.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.682 (0.463, 1.005)
	Treatment P-value [b]		0.05601
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

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Table AESV.KM.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Lipase increased	No. of Events (%)	8 (2.7)	5 (1.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.628 (0.531, 4.990)
	Treatment P-value [b]		0.38930
	Homogeneity P-value [c]		NA
Lymphocyte count decreased	No. of Events (%)	9 (3.0)	12 (4.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.746 (0.314, 1.776)
	Treatment P-value [b]		0.50674
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESV.KM.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Neutrophil count decreased	No. of Events (%)	21 (7.1)	43 (14.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.414 (0.245, 0.700)
	Treatment P-value [b]		0.00075
	Homogeneity P-value [c]		NA
White blood cell count decreased	No. of Events (%)	4 (1.4)	21 (7.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.181 (0.062, 0.527)
	Treatment P-value [b]		0.00043
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESV.KM.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Metabolism and nutrition disorders	No. of Events (%)	67 (22.6)	32 (11.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.087 (1.368, 3.183)
	Treatment P-value [b]		0.00047
	Homogeneity P-value [c]		NA
Decreased appetite	No. of Events (%)	16 (5.4)	7 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.209 (0.907, 5.379)
	Treatment P-value [b]		0.07328
	Homogeneity P-value [c]		NA

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

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Table AESV.KM.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Hyperglycaemia	No. of Events (%)	21 (7.1)	2 (0.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		10.395 (2.436, 44.354)
	Treatment P-value [b]		0.00008
	Homogeneity P-value [c]		NA
Hyponatraemia	No. of Events (%)	12 (4.1)	7 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.543 (0.605, 3.938)
	Treatment P-value [b]		0.35924
	Homogeneity P-value [c]		NA

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The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

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Table AESV.KM.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Musculoskeletal and connective tissue disorders	No. of Events (%)	10 (3.4)	15 (5.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.616 (0.277, 1.373)
	Treatment P-value [b]		0.23254
	Homogeneity P-value [c]		NA
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	No. of Events (%)	19 (6.4)	18 (6.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.006 (0.526, 1.923)
	Treatment P-value [b]		0.98517
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Analysis Plan: 15FEB2021 Confidential

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Table AESV.KM.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Malignant neoplasm progression	No. of Events (%)	12 (4.1)	11 (3.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.062 (0.466, 2.418)
	Treatment P-value [b]		0.88597
	Homogeneity P-value [c]		NA
Nervous system disorders	No. of Events (%)	23 (7.8)	13 (4.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.709 (0.864, 3.383)
	Treatment P-value [b]		0.11929
	Homogeneity P-value [c]		NA

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

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Table AESV.KM.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Peripheral sensory neuropathy	No. of Events (%)	10 (3.4)	7 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.381 (0.524, 3.642)
	Treatment P-value [b]		0.51203
	Homogeneity P-value [c]		NA
Renal and urinary disorders	No. of Events (%)	20 (6.8)	13 (4.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.445 (0.715, 2.919)
	Treatment P-value [b]		0.30216
	Homogeneity P-value [c]		NA

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

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Table AESV.KM.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Acute kidney injury	No. of Events (%)	8 (2.7)	3 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.514 (0.665, 9.502)
	Treatment P-value [b]		0.15958
	Homogeneity P-value [c]		NA
Haematuria	No. of Events (%)	6 (2.0)	4 (1.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.292 (0.358, 4.659)
	Treatment P-value [b]		0.69515
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

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Table AESV.KM.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	17 (5.7)	11 (3.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.496 (0.699, 3.204)
	Treatment P-value [b]		0.29619
	Homogeneity P-value [c]		NA
Skin and subcutaneous tissue disorders	No. of Events (%)	51 (17.2)	1 (0.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		56.180 (7.742, 407.667)
	Treatment P-value [b]		<.00001
	Homogeneity P-value [c]		NA

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

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Table AESV.KM.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Rash maculo-papular	No. of Events (%)	22 (7.4)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		<.00001
	Homogeneity P-value [c]		NA
Vascular disorders	No. of Events (%)	9 (3.0)	7 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.252 (0.466, 3.366)
	Treatment P-value [b]		0.65464
	Homogeneity P-value [c]		NA

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESV.KM.S1.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: <65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Any Event	No. of Events (%)	69 (65.1)	67 (65.0)
	Median Survival Est. (95% CI)	2.45 (1.81, 4.60)	1.45 (0.82, 2.69)
	Hazard Ratio (95% CI) [a]		0.817 (0.584, 1.144)
	Treatment P-value [b]		0.24681
	Interaction P-value [c]		0.21002
Blood and lymphatic system disorders	No. of Events (%)	15 (14.2)	19 (18.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.696 (0.354, 1.370)
	Treatment P-value [b]		0.30017
	Interaction P-value [c]		0.04660

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

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Table AESV.KM.S1.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: <65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Anaemia	No. of Events (%)	10 (9.4)	11 (10.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.829 (0.352, 1.952)
	Treatment P-value [b]		0.67858
	Interaction P-value [c]		0.13941
Febrile neutropenia	No. of Events (%)	0	5 (4.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.02154
	Interaction P-value [c]		0.98898

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Table AESV.KM.S1.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: <65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Infections and infestations	No. of Events (%)	16 (15.1)	11 (10.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.379 (0.640, 2.971)
	Treatment P-value [b]		0.40817
	Interaction P-value [c]		0.70274
Neutrophil count decreased	No. of Events (%)	5 (4.7)	15 (14.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.288 (0.105, 0.793)
	Treatment P-value [b]		0.01232
	Interaction P-value [c]		0.32247

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Table AESV.KM.S1.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: <65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
White blood cell count decreased	No. of Events (%)	0	7 (6.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00645
	Interaction P-value [c]		0.98801
Metabolism and nutrition disorders	No. of Events (%)	21 (19.8)	7 (6.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.954 (1.256, 6.948)
	Treatment P-value [b]		0.00910
	Interaction P-value [c]		0.39091

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Astellas: 7465-CL-0301
Table AESV.KM.S1.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: <65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Hyperglycaemia	No. of Events (%)	3 (2.8)	1 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.870 (0.299, 27.595)
	Treatment P-value [b]		0.34012
	Interaction P-value [c]		0.22766
Skin and subcutaneous tissue disorders	No. of Events (%)	14 (13.2)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00017
	Interaction P-value [c]		0.98746

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Table AESV.KM.S1.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: <65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Rash maculo-papular	No. of Events (%)	8 (7.5)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00569
	Interaction P-value [c]		1.00000

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

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Table AESV.KM.S1.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Any Event	No. of Events (%)	142 (74.7)	127 (67.6)
	Median Survival Est. (95% CI)	1.33 (0.92, 1.87)	1.51 (0.72, 2.53)
	Hazard Ratio (95% CI) [a]		1.065 (0.838, 1.353)
	Treatment P-value [b]		0.61705
	Interaction P-value [c]		0.21002
Blood and lymphatic system disorders	No. of Events (%)	17 (8.9)	51 (27.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.287 (0.166, 0.498)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.04660

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S1.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Anaemia	No. of Events (%)	9 (4.7)	24 (12.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.348 (0.162, 0.750)
	Treatment P-value [b]		0.00453
	Interaction P-value [c]		0.13941
Febrile neutropenia	No. of Events (%)	4 (2.1)	11 (5.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.351 (0.112, 1.103)
	Treatment P-value [b]		0.05992
	Interaction P-value [c]		0.98898

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Table AESV.KM.S1.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Infections and infestations	No. of Events (%)	36 (18.9)	22 (11.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.654 (0.973, 2.811)
	Treatment P-value [b]		0.06055
	Interaction P-value [c]		0.70274
Neutrophil count decreased	No. of Events (%)	16 (8.4)	28 (14.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.524 (0.283, 0.969)
	Treatment P-value [b]		0.03477
	Interaction P-value [c]		0.32247

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Analysis Plan: 15FEB2021 Confidential

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Table AESV.KM.S1.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
White blood cell count decreased	No. of Events (%)	4 (2.1)	14 (7.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.272 (0.089, 0.826)
	Treatment P-value [b]		0.01334
	Interaction P-value [c]		0.98801
Metabolism and nutrition disorders	No. of Events (%)	46 (24.2)	25 (13.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.920 (1.180, 3.125)
	Treatment P-value [b]		0.00786
	Interaction P-value [c]		0.39091

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Table AESV.KM.S1.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Hyperglycaemia	No. of Events (%)	18 (9.5)	1 (0.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		18.525 (2.473, 138.773)
	Treatment P-value [b]		0.00008
	Interaction P-value [c]		0.22766
Skin and subcutaneous tissue disorders	No. of Events (%)	37 (19.5)	1 (0.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		40.257 (5.523, 293.438)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.98746

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S1.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Rash maculo-papular	No. of Events (%)	14 (7.4)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00016
	Interaction P-value [c]		1.00000

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

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Table AESV.KM.S2.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Any Event	No. of Events (%)	169 (69.0)	154 (68.1)
	Median Survival Est. (95% CI)	1.91 (1.45, 2.79)	1.41 (0.82, 2.10)
	Hazard Ratio (95% CI) [a]		0.862 (0.693, 1.073)
	Treatment P-value [b]		0.21445
	Interaction P-value [c]		0.01310
Blood and lymphatic system disorders	No. of Events (%)	30 (12.2)	53 (23.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.463 (0.296, 0.725)
	Treatment P-value [b]		0.00054
	Interaction P-value [c]		0.10532

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S2.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Anaemia	No. of Events (%)	18 (7.3)	28 (12.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.548 (0.303, 0.991)
	Treatment P-value [b]		0.04334
	Interaction P-value [c]		0.31629
Febrile neutropenia	No. of Events (%)	4 (1.6)	10 (4.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.355 (0.111, 1.132)
	Treatment P-value [b]		0.06606
	Interaction P-value [c]		0.98869

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S2.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Infections and infestations	No. of Events (%)	40 (16.3)	30 (13.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.196 (0.745, 1.920)
	Treatment P-value [b]		0.45742
	Interaction P-value [c]		0.02225
Neutrophil count decreased	No. of Events (%)	20 (8.2)	35 (15.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.473 (0.273, 0.819)
	Treatment P-value [b]		0.00656
	Interaction P-value [c]		0.30562

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S2.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
White blood cell count decreased	No. of Events (%)	3 (1.2)	18 (8.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.145 (0.043, 0.492)
	Treatment P-value [b]		0.00033
	Interaction P-value [c]		0.41616
Metabolism and nutrition disorders	No. of Events (%)	52 (21.2)	22 (9.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.225 (1.352, 3.664)
	Treatment P-value [b]		0.00123
	Interaction P-value [c]		0.94473

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S2.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Hyperglycaemia	No. of Events (%)	15 (6.1)	1 (0.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		14.011 (1.851, 106.066)
	Treatment P-value [b]		0.00078
	Interaction P-value [c]		0.70660
Skin and subcutaneous tissue disorders	No. of Events (%)	42 (17.1)	1 (0.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		41.031 (5.647, 298.131)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.98922

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S2.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Rash maculo-papular	No. of Events (%)	17 (6.9)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00008
	Interaction P-value [c]		0.99989

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table AESV.KM.S2.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Any Event	No. of Events (%)	42 (82.4)	40 (61.5)
	Median Survival Est. (95% CI)	0.66 (0.53, 1.77)	2.33 (0.69, 5.78)
	Hazard Ratio (95% CI) [a]		1.594 (1.033, 2.459)
	Treatment P-value [b]		0.04365
	Interaction P-value [c]		0.01310
Blood and lymphatic system disorders	No. of Events (%)	2 (3.9)	17 (26.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (12.94, NC)
	Hazard Ratio (95% CI) [a]		0.131 (0.030, 0.565)
	Treatment P-value [b]		0.00152
	Interaction P-value [c]		0.10532

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AESV.KM.S2.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Anaemia	No. of Events (%)	1 (2.0)	7 (10.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.180 (0.022, 1.462)
	Treatment P-value [b]		0.07090
	Interaction P-value [c]		0.31629
Febrile neutropenia	No. of Events (%)	0	6 (9.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.02741
	Interaction P-value [c]		0.98869

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table AESV.KM.S2.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Infections and infestations	No. of Events (%)	12 (23.5)	3 (4.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.781 (1.631, 20.489)
	Treatment P-value [b]		0.00192
	Interaction P-value [c]		0.02225
Neutrophil count decreased	No. of Events (%)	1 (2.0)	8 (12.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.154 (0.019, 1.229)
	Treatment P-value [b]		0.04276
	Interaction P-value [c]		0.30562

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table AESV.KM.S2.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
White blood cell count decreased	No. of Events (%)	1 (2.0)	3 (4.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.421 (0.044, 4.051)
	Treatment P-value [b]		0.44469
	Interaction P-value [c]		0.41616
Metabolism and nutrition disorders	No. of Events (%)	15 (29.4)	10 (15.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.152 (0.967, 4.792)
	Treatment P-value [b]		0.05484
	Interaction P-value [c]		0.94473

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S2.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Hyperglycaemia	No. of Events (%)	6 (11.8)	1 (1.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.983 (0.961, 66.318)
	Treatment P-value [b]		0.02352
	Interaction P-value [c]		0.70660
Skin and subcutaneous tissue disorders	No. of Events (%)	9 (17.6)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00040
	Interaction P-value [c]		0.98922

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S2.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Rash maculo-papular	No. of Events (%)	5 (9.8)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00951
	Interaction P-value [c]		0.99989

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Analysis Plan: 15FEB2021 Confidential

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Table AESV.KM.S3.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Any Event	No. of Events (%)	166 (70.9)	149 (68.0)
	Median Survival Est. (95% CI)	1.81 (1.18, 2.27)	1.41 (0.79, 2.10)
	Hazard Ratio (95% CI) [a]		0.925 (0.741, 1.154)
	Treatment P-value [b]		0.50198
	Interaction P-value [c]		0.43346
Blood and lymphatic system disorders	No. of Events (%)	24 (10.3)	55 (25.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.349 (0.216, 0.564)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.27295

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S3.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Anaemia	No. of Events (%)	12 (5.1)	22 (10.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.473 (0.234, 0.957)
	Treatment P-value [b]		0.03690
	Interaction P-value [c]		0.66410
Febrile neutropenia	No. of Events (%)	2 (0.9)	15 (6.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.118 (0.027, 0.517)
	Treatment P-value [b]		0.00073
	Interaction P-value [c]		0.03720

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S3.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Infections and infestations	No. of Events (%)	42 (17.9)	27 (12.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.451 (0.895, 2.353)
	Treatment P-value [b]		0.13230
	Interaction P-value [c]		0.58318
Neutrophil count decreased	No. of Events (%)	13 (5.6)	29 (13.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.381 (0.198, 0.732)
	Treatment P-value [b]		0.00279
	Interaction P-value [c]		0.37700

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S3.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
White blood cell count decreased	No. of Events (%)	3 (1.3)	12 (5.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.225 (0.063, 0.796)
	Treatment P-value [b]		0.01164
	Interaction P-value [c]		0.61517
Metabolism and nutrition disorders	No. of Events (%)	51 (21.8)	25 (11.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.971 (1.221, 3.180)
	Treatment P-value [b]		0.00475
	Interaction P-value [c]		0.48291

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table AESV.KM.S3.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Hyperglycaemia	No. of Events (%)	19 (8.1)	2 (0.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.025 (2.102, 38.746)
	Treatment P-value [b]		0.00032
	Interaction P-value [c]		0.99208
Skin and subcutaneous tissue disorders	No. of Events (%)	42 (17.9)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.98623

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table AESV.KM.S3.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Rash maculo-papular	No. of Events (%)	18 (7.7)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00004
	Interaction P-value [c]		0.99995

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table AESV.KM.S3.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Any Event	No. of Events (%)	45 (72.6)	45 (62.5)
	Median Survival Est. (95% CI)	1.74 (0.82, 3.02)	2.17 (0.72, 5.68)
	Hazard Ratio (95% CI) [a]		1.115 (0.738, 1.686)
	Treatment P-value [b]		0.54473
	Interaction P-value [c]		0.43346
Blood and lymphatic system disorders	No. of Events (%)	8 (12.9)	15 (20.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.605 (0.256, 1.426)
	Treatment P-value [b]		0.25112
	Interaction P-value [c]		0.27295

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S3.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Anaemia	No. of Events (%)	7 (11.3)	13 (18.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.612 (0.244, 1.533)
	Treatment P-value [b]		0.28247
	Interaction P-value [c]		0.66410
Febrile neutropenia	No. of Events (%)	2 (3.2)	1 (1.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.362 (0.214, 26.051)
	Treatment P-value [b]		0.44672
	Interaction P-value [c]		0.03720

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table AESV.KM.S3.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Infections and infestations	No. of Events (%)	10 (16.1)	6 (8.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.986 (0.722, 5.464)
	Treatment P-value [b]		0.17759
	Interaction P-value [c]		0.58318
Neutrophil count decreased	No. of Events (%)	8 (12.9)	14 (19.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.621 (0.261, 1.482)
	Treatment P-value [b]		0.29652
	Interaction P-value [c]		0.37700

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table AESV.KM.S3.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
White blood cell count decreased	No. of Events (%)	1 (1.6)	9 (12.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.121 (0.015, 0.952)
	Treatment P-value [b]		0.01682
	Interaction P-value [c]		0.61517
Metabolism and nutrition disorders	No. of Events (%)	16 (25.8)	7 (9.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.828 (1.163, 6.875)
	Treatment P-value [b]		0.01919
	Interaction P-value [c]		0.48291

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Astellas: 7465-CL-0301
Table AESV.KM.S3.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Hyperglycaemia	No. of Events (%)	2 (3.2)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.12596
	Interaction P-value [c]		0.99208
Skin and subcutaneous tissue disorders	No. of Events (%)	9 (14.5)	1 (1.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		11.082 (1.404, 87.481)
	Treatment P-value [b]		0.00409
	Interaction P-value [c]		0.98623

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S3.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Rash maculo-papular	No. of Events (%)	4 (6.5)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.02798
	Interaction P-value [c]		0.99995

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESV.KM.S4.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Western Europe

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Any Event	No. of Events (%)	80 (65.6)	83 (67.5)
	Median Survival Est. (95% CI)	2.79 (1.87, 4.93)	1.61 (0.59, 2.50)
	Hazard Ratio (95% CI) [a]		0.782 (0.575, 1.063)
	Treatment P-value [b]		0.13132
	Interaction P-value [c]		0.06395
Blood and lymphatic system disorders	No. of Events (%)	7 (5.7)	24 (19.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.252 (0.108, 0.584)
	Treatment P-value [b]		0.00065
	Interaction P-value [c]		0.35296

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S4.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Western Europe

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Anaemia	No. of Events (%)	2 (1.6)	8 (6.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.234 (0.050, 1.101)
	Treatment P-value [b]		0.04779
	Interaction P-value [c]		0.06107
Febrile neutropenia	No. of Events (%)	0	6 (4.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.01257
	Interaction P-value [c]		0.99987

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S4.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Western Europe

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Infections and infestations	No. of Events (%)	20 (16.4)	16 (13.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.216 (0.630, 2.346)
	Treatment P-value [b]		0.55572
	Interaction P-value [c]		0.61437
Neutrophil count decreased	No. of Events (%)	1 (0.8)	7 (5.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.138 (0.017, 1.119)
	Treatment P-value [b]		0.02445
	Interaction P-value [c]		0.48443

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S4.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Western Europe

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
White blood cell count decreased	No. of Events (%)	0	2 (1.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.15300
	Interaction P-value [c]		0.90745
Metabolism and nutrition disorders	No. of Events (%)	20 (16.4)	12 (9.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.616 (0.790, 3.305)
	Treatment P-value [b]		0.17982
	Interaction P-value [c]		0.62026

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S4.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Western Europe

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Hyperglycaemia	No. of Events (%)	10 (8.2)	1 (0.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.966 (1.276, 77.857)
	Treatment P-value [b]		0.00646
	Interaction P-value [c]		0.94516
Skin and subcutaneous tissue disorders	No. of Events (%)	17 (13.9)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00003
	Interaction P-value [c]		0.99983

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S4.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Western Europe

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Rash maculo-papular	No. of Events (%)	6 (4.9)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.01596
	Interaction P-value [c]		1.00000

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S4.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Any Event	No. of Events (%)	33 (78.6)	24 (61.5)
	Median Survival Est. (95% CI)	0.67 (0.46, 1.41)	2.10 (0.66, NC)
	Hazard Ratio (95% CI) [a]		1.607 (0.949, 2.720)
	Treatment P-value [b]		0.08305
	Interaction P-value [c]		0.06395
Blood and lymphatic system disorders	No. of Events (%)	4 (9.5)	10 (25.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.339 (0.106, 1.081)
	Treatment P-value [b]		0.05530
	Interaction P-value [c]		0.35296

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S4.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Anaemia	No. of Events (%)	1 (2.4)	9 (23.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.091 (0.011, 0.716)
	Treatment P-value [b]		0.00491
	Interaction P-value [c]		0.06107
Febrile neutropenia	No. of Events (%)	1 (2.4)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.33523
	Interaction P-value [c]		0.99987

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S4.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Infections and infestations	No. of Events (%)	7 (16.7)	4 (10.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.679 (0.492, 5.736)
	Treatment P-value [b]		0.41693
	Interaction P-value [c]		0.61437
Neutrophil count decreased	No. of Events (%)	3 (7.1)	7 (17.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.359 (0.093, 1.390)
	Treatment P-value [b]		0.12059
	Interaction P-value [c]		0.48443

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table AESV.KM.S4.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
White blood cell count decreased	No. of Events (%)	1 (2.4)	3 (7.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.304 (0.032, 2.923)
	Treatment P-value [b]		0.27179
	Interaction P-value [c]		0.90745
Metabolism and nutrition disorders	No. of Events (%)	15 (35.7)	6 (15.4)
	Median Survival Est. (95% CI)	NC (8.57, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.684 (1.041, 6.919)
	Treatment P-value [b]		0.03944
	Interaction P-value [c]		0.62026

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table AESV.KM.S4.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Hyperglycaemia	No. of Events (%)	5 (11.9)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.02718
	Interaction P-value [c]		0.94516
Skin and subcutaneous tissue disorders	No. of Events (%)	12 (28.6)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00035
	Interaction P-value [c]		0.99983

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AESV.KM.S4.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Rash maculo-papular	No. of Events (%)	12 (28.6)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00035
	Interaction P-value [c]		1.00000

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
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Astellas: 7465-CL-0301
Table AESV.KM.S4.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Any Event	No. of Events (%)	98 (74.2)	87 (67.4)
	Median Survival Est. (95% CI)	1.43 (0.95, 2.07)	1.41 (0.53, 2.63)
	Hazard Ratio (95% CI) [a]		1.012 (0.758, 1.351)
	Treatment P-value [b]		0.89806
	Interaction P-value [c]		0.06395
Blood and lymphatic system disorders	No. of Events (%)	21 (15.9)	36 (27.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (12.94, NC)
	Hazard Ratio (95% CI) [a]		0.515 (0.301, 0.882)
	Treatment P-value [b]		0.01296
	Interaction P-value [c]		0.35296

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Analysis Plan: 15FEB2021 Confidential

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Table AESV.KM.S4.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Anaemia	No. of Events (%)	16 (12.1)	18 (14.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.842 (0.429, 1.651)
	Treatment P-value [b]		0.60530
	Interaction P-value [c]		0.06107
Febrile neutropenia	No. of Events (%)	3 (2.3)	10 (7.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.285 (0.078, 1.034)
	Treatment P-value [b]		0.04126
	Interaction P-value [c]		0.99987

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table AESV.KM.S4.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Infections and infestations	No. of Events (%)	25 (18.9)	13 (10.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.941 (0.993, 3.795)
	Treatment P-value [b]		0.04554
	Interaction P-value [c]		0.61437
Neutrophil count decreased	No. of Events (%)	17 (12.9)	29 (22.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.501 (0.275, 0.912)
	Treatment P-value [b]		0.02551
	Interaction P-value [c]		0.48443

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table AESV.KM.S4.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
White blood cell count decreased	No. of Events (%)	3 (2.3)	16 (12.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.170 (0.050, 0.585)
	Treatment P-value [b]		0.00153
	Interaction P-value [c]		0.90745
Metabolism and nutrition disorders	No. of Events (%)	32 (24.2)	14 (10.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.416 (1.289, 4.528)
	Treatment P-value [b]		0.00439
	Interaction P-value [c]		0.62026

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table AESV.KM.S4.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Hyperglycaemia	No. of Events (%)	6 (4.5)	1 (0.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.013 (0.724, 49.944)
	Treatment P-value [b]		0.05972
	Interaction P-value [c]		0.94516
Skin and subcutaneous tissue disorders	No. of Events (%)	22 (16.7)	1 (0.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		23.590 (3.180, 175.018)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.99983

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S4.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Rash maculo-papular	No. of Events (%)	4 (3.0)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.04591
	Interaction P-value [c]		1.00000

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table AESV.KM.S5.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Any Event	No. of Events (%)	74 (61.7)	69 (58.0)
	Median Survival Est. (95% CI)	2.43 (1.45, 5.16)	2.17 (0.95, 6.90)
	Hazard Ratio (95% CI) [a]		0.949 (0.683, 1.317)
	Treatment P-value [b]		0.71924
	Interaction P-value [c]		0.87195
Blood and lymphatic system disorders	No. of Events (%)	9 (7.5)	20 (16.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.425 (0.194, 0.933)
	Treatment P-value [b]		0.02808
	Interaction P-value [c]		0.78611

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

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Table AESV.KM.S5.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Anaemia	No. of Events (%)	4 (3.3)	9 (7.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.430 (0.132, 1.395)
	Treatment P-value [b]		0.15180
	Interaction P-value [c]		0.79759
Febrile neutropenia	No. of Events (%)	2 (1.7)	3 (2.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.664 (0.111, 3.973)
	Treatment P-value [b]		0.65810
	Interaction P-value [c]		0.19076

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Subgroup: ECOG PS from IRT Strata, Level: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Infections and infestations	No. of Events (%)	15 (12.5)	12 (10.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.219 (0.571, 2.604)
	Treatment P-value [b]		0.60551
	Interaction P-value [c]		0.44147
Neutrophil count decreased	No. of Events (%)	9 (7.5)	29 (24.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.267 (0.126, 0.564)
	Treatment P-value [b]		0.00025
	Interaction P-value [c]		0.04700

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table AESV.KM.S5.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
White blood cell count decreased	No. of Events (%)	3 (2.5)	14 (11.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.199 (0.057, 0.693)
	Treatment P-value [b]		0.00498
	Interaction P-value [c]		0.75332
Metabolism and nutrition disorders	No. of Events (%)	25 (20.8)	9 (7.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.989 (1.395, 6.403)
	Treatment P-value [b]		0.00380
	Interaction P-value [c]		0.27549

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Subgroup: ECOG PS from IRT Strata, Level: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Hyperglycaemia	No. of Events (%)	8 (6.7)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00420
	Interaction P-value [c]		0.98857
Skin and subcutaneous tissue disorders	No. of Events (%)	27 (22.5)	1 (0.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		30.696 (4.171, 225.929)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.98430

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: ECOG PS from IRT Strata, Level: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Rash maculo-papular	No. of Events (%)	10 (8.3)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00125
	Interaction P-value [c]		0.99995

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Table AESV.KM.S5.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Any Event	No. of Events (%)	137 (77.8)	125 (72.7)
	Median Survival Est. (95% CI)	1.38 (0.95, 1.87)	1.30 (0.66, 2.04)
	Hazard Ratio (95% CI) [a]		0.981 (0.770, 1.250)
	Treatment P-value [b]		0.96622
	Interaction P-value [c]		0.87195
Blood and lymphatic system disorders	No. of Events (%)	23 (13.1)	50 (29.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.374 (0.228, 0.613)
	Treatment P-value [b]		0.00005
	Interaction P-value [c]		0.78611

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table AESV.KM.S5.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Anaemia	No. of Events (%)	15 (8.5)	26 (15.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.512 (0.271, 0.967)
	Treatment P-value [b]		0.03426
	Interaction P-value [c]		0.79759
Febrile neutropenia	No. of Events (%)	2 (1.1)	13 (7.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.140 (0.032, 0.622)
	Treatment P-value [b]		0.00288
	Interaction P-value [c]		0.19076

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Astellas: 7465-CL-0301
Table AESV.KM.S5.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Infections and infestations	No. of Events (%)	37 (21.0)	21 (12.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.756 (1.028, 3.000)
	Treatment P-value [b]		0.03646
	Interaction P-value [c]		0.44147
Neutrophil count decreased	No. of Events (%)	12 (6.8)	14 (8.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.793 (0.367, 1.715)
	Treatment P-value [b]		0.52281
	Interaction P-value [c]		0.04700

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S5.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
White blood cell count decreased	No. of Events (%)	1 (0.6)	7 (4.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.135 (0.017, 1.095)
	Treatment P-value [b]		0.02850
	Interaction P-value [c]		0.75332
Metabolism and nutrition disorders	No. of Events (%)	42 (23.9)	23 (13.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.795 (1.080, 2.985)
	Treatment P-value [b]		0.02270
	Interaction P-value [c]		0.27549

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table AESV.KM.S5.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Hyperglycaemia	No. of Events (%)	13 (7.4)	2 (1.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.397 (1.443, 28.346)
	Treatment P-value [b]		0.00507
	Interaction P-value [c]		0.98857
Skin and subcutaneous tissue disorders	No. of Events (%)	24 (13.6)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.98430

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table AESV.KM.S5.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Rash maculo-papular	No. of Events (%)	12 (6.8)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00067
	Interaction P-value [c]		0.99995

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table AESV.KM.S6.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Any Event	No. of Events (%)	70 (76.1)	56 (64.4)
	Median Survival Est. (95% CI)	0.95 (0.62, 2.14)	1.68 (0.72, 2.79)
	Hazard Ratio (95% CI) [a]		1.202 (0.846, 1.709)
	Treatment P-value [b]		0.30774
	Interaction P-value [c]		0.14804
Blood and lymphatic system disorders	No. of Events (%)	10 (10.9)	16 (18.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.530 (0.241, 1.168)
	Treatment P-value [b]		0.12252
	Interaction P-value [c]		0.40825

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S6.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Anaemia	No. of Events (%)	6 (6.5)	5 (5.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.094 (0.334, 3.585)
	Treatment P-value [b]		0.85672
	Interaction P-value [c]		0.14741
Febrile neutropenia	No. of Events (%)	2 (2.2)	6 (6.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.305 (0.062, 1.514)
	Treatment P-value [b]		0.13327
	Interaction P-value [c]		0.68061

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S6.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Infections and infestations	No. of Events (%)	21 (22.8)	14 (16.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.455 (0.740, 2.861)
	Treatment P-value [b]		0.27004
	Interaction P-value [c]		0.80939
Neutrophil count decreased	No. of Events (%)	8 (8.7)	7 (8.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.034 (0.375, 2.852)
	Treatment P-value [b]		0.95825
	Interaction P-value [c]		0.05692

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S6.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
White blood cell count decreased	No. of Events (%)	0	3 (3.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.07645
	Interaction P-value [c]		0.99018
Metabolism and nutrition disorders	No. of Events (%)	23 (25.0)	10 (11.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.352 (1.119, 4.942)
	Treatment P-value [b]		0.01870
	Interaction P-value [c]		0.75966

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table AESV.KM.S6.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Hyperglycaemia	No. of Events (%)	6 (6.5)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.01521
	Interaction P-value [c]		0.99047
Skin and subcutaneous tissue disorders	No. of Events (%)	17 (18.5)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00003
	Interaction P-value [c]		0.98787

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S6.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Rash maculo-papular	No. of Events (%)	10 (10.9)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00168
	Interaction P-value [c]		0.99981

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table AESV.KM.S6.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Any Event	No. of Events (%)	141 (69.1)	138 (67.6)
	Median Survival Est. (95% CI)	1.87 (1.45, 2.79)	1.41 (0.69, 2.33)
	Hazard Ratio (95% CI) [a]		0.880 (0.696, 1.113)
	Treatment P-value [b]		0.32179
	Interaction P-value [c]		0.14804
Blood and lymphatic system disorders	No. of Events (%)	22 (10.8)	54 (26.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.358 (0.218, 0.587)
	Treatment P-value [b]		0.00002
	Interaction P-value [c]		0.40825

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S6.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Anaemia	No. of Events (%)	13 (6.4)	30 (14.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.402 (0.210, 0.771)
	Treatment P-value [b]		0.00442
	Interaction P-value [c]		0.14741
Febrile neutropenia	No. of Events (%)	2 (1.0)	10 (4.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.192 (0.042, 0.877)
	Treatment P-value [b]		0.01712
	Interaction P-value [c]		0.68061

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S6.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Infections and infestations	No. of Events (%)	31 (15.2)	19 (9.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.622 (0.917, 2.872)
	Treatment P-value [b]		0.09211
	Interaction P-value [c]		0.80939
Neutrophil count decreased	No. of Events (%)	13 (6.4)	36 (17.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.323 (0.171, 0.610)
	Treatment P-value [b]		0.00026
	Interaction P-value [c]		0.05692

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AESV.KM.S6.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
White blood cell count decreased	No. of Events (%)	4 (2.0)	18 (8.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.209 (0.071, 0.618)
	Treatment P-value [b]		0.00181
	Interaction P-value [c]		0.99018
Metabolism and nutrition disorders	No. of Events (%)	44 (21.6)	22 (10.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.043 (1.225, 3.408)
	Treatment P-value [b]		0.00495
	Interaction P-value [c]		0.75966

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AESV.KM.S6.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Hyperglycaemia	No. of Events (%)	15 (7.4)	2 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.559 (1.729, 33.055)
	Treatment P-value [b]		0.00151
	Interaction P-value [c]		0.99047
Skin and subcutaneous tissue disorders	No. of Events (%)	34 (16.7)	1 (0.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		36.393 (4.982, 265.868)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.98787

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Analysis Plan: 15FEB2021 Confidential

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Table AESV.KM.S6.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Rash maculo-papular	No. of Events (%)	12 (5.9)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00052
	Interaction P-value [c]		0.99981

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Astellas: 7465-CL-0301
Table AESV.KM.S7.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Any Event	No. of Events (%)	101 (72.1)	59 (55.1)
	Median Survival Est. (95% CI)	1.71 (1.12, 2.73)	4.96 (2.69, NC)
	Hazard Ratio (95% CI) [a]		1.500 (1.088, 2.069)
	Treatment P-value [b]		0.00716
	Interaction P-value [c]		0.00194
Blood and lymphatic system disorders	No. of Events (%)	18 (12.9)	18 (16.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.733 (0.381, 1.408)
	Treatment P-value [b]		0.31575
	Interaction P-value [c]		0.07395

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AESV.KM.S7.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Anaemia	No. of Events (%)	15 (10.7)	9 (8.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.235 (0.540, 2.822)
	Treatment P-value [b]		0.63178
	Interaction P-value [c]		0.01398
Infections and infestations	No. of Events (%)	29 (20.7)	10 (9.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.264 (1.103, 4.647)
	Treatment P-value [b]		0.02092
	Interaction P-value [c]		0.30064

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AESV.KM.S7.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Neutrophil count decreased	No. of Events (%)	14 (10.0)	10 (9.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.038 (0.461, 2.338)
	Treatment P-value [b]		0.94909
	Interaction P-value [c]		0.02999
White blood cell count decreased	No. of Events (%)	1 (0.7)	1 (0.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.759 (0.047, 12.128)
	Treatment P-value [b]		0.83621
	Interaction P-value [c]		0.67507

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Table AESV.KM.S7.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Metabolism and nutrition disorders	No. of Events (%)	33 (23.6)	3 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.286 (2.849, 30.268)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.00779
Hyperglycaemia	No. of Events (%)	10 (7.1)	1 (0.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.748 (0.992, 60.526)
	Treatment P-value [b]		0.02104
	Interaction P-value [c]		0.99208

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Table AESV.KM.S7.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Skin and subcutaneous tissue disorders	No. of Events (%)	28 (20.0)	1 (0.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		22.975 (3.126, 168.873)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.99976
Rash maculo-papular	No. of Events (%)	12 (8.6)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00218
	Interaction P-value [c]		1.00000

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Table AESV.KM.S7.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Any Event	No. of Events (%)	61 (71.8)	79 (72.5)
	Median Survival Est. (95% CI)	1.18 (0.72, 1.91)	0.72 (0.26, 1.45)
	Hazard Ratio (95% CI) [a]		0.818 (0.585, 1.142)
	Treatment P-value [b]		0.22315
	Interaction P-value [c]		0.00194
Blood and lymphatic system disorders	No. of Events (%)	9 (10.6)	32 (29.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.307 (0.146, 0.642)
	Treatment P-value [b]		0.00106
	Interaction P-value [c]		0.07395

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Table AESV.KM.S7.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Anaemia	No. of Events (%)	2 (2.4)	21 (19.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.107 (0.025, 0.457)
	Treatment P-value [b]		0.00026
	Interaction P-value [c]		0.01398
Infections and infestations	No. of Events (%)	13 (15.3)	16 (14.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.006 (0.484, 2.091)
	Treatment P-value [b]		0.99140
	Interaction P-value [c]		0.30064

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S7.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Neutrophil count decreased	No. of Events (%)	6 (7.1)	28 (25.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.221 (0.092, 0.535)
	Treatment P-value [b]		0.00043
	Interaction P-value [c]		0.02999
White blood cell count decreased	No. of Events (%)	3 (3.5)	18 (16.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.193 (0.057, 0.654)
	Treatment P-value [b]		0.00349
	Interaction P-value [c]		0.67507

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Table AESV.KM.S7.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Metabolism and nutrition disorders	No. of Events (%)	21 (24.7)	16 (14.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.752 (0.914, 3.358)
	Treatment P-value [b]		0.09112
	Interaction P-value [c]		0.00779
Hyperglycaemia	No. of Events (%)	5 (5.9)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.01046
	Interaction P-value [c]		0.99208

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Skin and subcutaneous tissue disorders	No. of Events (%)	16 (18.8)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.99976
Rash maculo-papular	No. of Events (%)	7 (8.2)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00266
	Interaction P-value [c]		1.00000

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S7.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Any Event	No. of Events (%)	49 (69.0)	56 (74.7)
	Median Survival Est. (95% CI)	2.10 (1.25, 4.93)	0.46 (0.30, 1.61)
	Hazard Ratio (95% CI) [a]		0.643 (0.438, 0.943)
	Treatment P-value [b]		0.02553
	Interaction P-value [c]		0.00194
Blood and lymphatic system disorders	No. of Events (%)	5 (7.0)	20 (26.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.218 (0.082, 0.580)
	Treatment P-value [b]		0.00104
	Interaction P-value [c]		0.07395

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AESV.KM.S7.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Anaemia	No. of Events (%)	2 (2.8)	5 (6.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.412 (0.080, 2.125)
	Treatment P-value [b]		0.27725
	Interaction P-value [c]		0.01398
Infections and infestations	No. of Events (%)	10 (14.1)	7 (9.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.548 (0.589, 4.067)
	Treatment P-value [b]		0.38200
	Interaction P-value [c]		0.30064

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S7.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Neutrophil count decreased	No. of Events (%)	1 (1.4)	5 (6.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.208 (0.024, 1.782)
	Treatment P-value [b]		0.10734
	Interaction P-value [c]		0.02999
White blood cell count decreased	No. of Events (%)	0	2 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.16165
	Interaction P-value [c]		0.67507

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S7.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Metabolism and nutrition disorders	No. of Events (%)	13 (18.3)	13 (17.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.992 (0.460, 2.141)
	Treatment P-value [b]		0.99936
	Interaction P-value [c]		0.00779
Hyperglycaemia	No. of Events (%)	6 (8.5)	1 (1.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.415 (0.772, 53.287)
	Treatment P-value [b]		0.04510
	Interaction P-value [c]		0.99208

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S7.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Skin and subcutaneous tissue disorders	No. of Events (%)	7 (9.9)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00527
	Interaction P-value [c]		0.99976
Rash maculo-papular	No. of Events (%)	3 (4.2)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.07663
	Interaction P-value [c]		1.00000

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Analysis Plan: 15FEB2021 Confidential

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Table AESV.KM.S8.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Any Event	No. of Events (%)	74 (77.1)	66 (64.7)
	Median Survival Est. (95% CI)	1.25 (0.72, 2.33)	1.71 (0.66, 2.79)
	Hazard Ratio (95% CI) [a]		1.145 (0.822, 1.596)
	Treatment P-value [b]		0.41921
	Interaction P-value [c]		0.22635
Blood and lymphatic system disorders	No. of Events (%)	16 (16.7)	22 (21.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.709 (0.372, 1.350)
	Treatment P-value [b]		0.29388
	Interaction P-value [c]		0.02936

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S8.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Anaemia	No. of Events (%)	11 (11.5)	10 (9.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.152 (0.489, 2.712)
	Treatment P-value [b]		0.73900
	Interaction P-value [c]		0.01687
Febrile neutropenia	No. of Events (%)	3 (3.1)	7 (6.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.440 (0.114, 1.703)
	Treatment P-value [b]		0.22070
	Interaction P-value [c]		0.24274

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S8.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Infections and infestations	No. of Events (%)	14 (14.6)	10 (9.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.491 (0.662, 3.355)
	Treatment P-value [b]		0.33501
	Interaction P-value [c]		0.91768
Neutrophil count decreased	No. of Events (%)	10 (10.4)	19 (18.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.509 (0.237, 1.096)
	Treatment P-value [b]		0.08410
	Interaction P-value [c]		0.63814

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S8.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
White blood cell count decreased	No. of Events (%)	1 (1.0)	9 (8.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.111 (0.014, 0.876)
	Treatment P-value [b]		0.01194
	Interaction P-value [c]		0.56225
Metabolism and nutrition disorders	No. of Events (%)	24 (25.0)	11 (10.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.418 (1.184, 4.936)
	Treatment P-value [b]		0.01358
	Interaction P-value [c]		0.68174

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Hyperglycaemia	No. of Events (%)	6 (6.3)	1 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.402 (0.771, 53.178)
	Treatment P-value [b]		0.05038
	Interaction P-value [c]		0.58242
Skin and subcutaneous tissue disorders	No. of Events (%)	21 (21.9)	1 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		24.696 (3.322, 183.621)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.98242

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Rash maculo-papular	No. of Events (%)	10 (10.4)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00095
	Interaction P-value [c]		0.99983

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
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Table AESV.KM.S8.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Any Event	No. of Events (%)	137 (68.5)	128 (67.7)
	Median Survival Est. (95% CI)	1.87 (1.41, 2.79)	1.41 (0.79, 2.50)
	Hazard Ratio (95% CI) [a]		0.889 (0.699, 1.131)
	Treatment P-value [b]		0.35569
	Interaction P-value [c]		0.22635
Blood and lymphatic system disorders	No. of Events (%)	16 (8.0)	48 (25.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.273 (0.155, 0.481)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.02936

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table AESV.KM.S8.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Anaemia	No. of Events (%)	8 (4.0)	25 (13.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.277 (0.125, 0.614)
	Treatment P-value [b]		0.00063
	Interaction P-value [c]		0.01687
Febrile neutropenia	No. of Events (%)	1 (0.5)	9 (4.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.101 (0.013, 0.798)
	Treatment P-value [b]		0.00754
	Interaction P-value [c]		0.24274

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table AESV.KM.S8.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Infections and infestations	No. of Events (%)	38 (19.0)	23 (12.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.568 (0.934, 2.632)
	Treatment P-value [b]		0.08749
	Interaction P-value [c]		0.91768
Neutrophil count decreased	No. of Events (%)	11 (5.5)	24 (12.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.396 (0.194, 0.809)
	Treatment P-value [b]		0.00887
	Interaction P-value [c]		0.63814

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table AESV.KM.S8.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
White blood cell count decreased	No. of Events (%)	3 (1.5)	12 (6.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.227 (0.064, 0.805)
	Treatment P-value [b]		0.01227
	Interaction P-value [c]		0.56225
Metabolism and nutrition disorders	No. of Events (%)	43 (21.5)	21 (11.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.010 (1.193, 3.386)
	Treatment P-value [b]		0.00740
	Interaction P-value [c]		0.68174

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Table AESV.KM.S8.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Hyperglycaemia	No. of Events (%)	15 (7.5)	1 (0.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		14.560 (1.924, 110.189)
	Treatment P-value [b]		0.00056
	Interaction P-value [c]		0.58242
Skin and subcutaneous tissue disorders	No. of Events (%)	30 (15.0)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.98242

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S8.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Rash maculo-papular	No. of Events (%)	12 (6.0)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00075
	Interaction P-value [c]		0.99983

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Astellas: 7465-CL-0301
Table AESV.KM.S9.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Any Event	No. of Events (%)	185 (71.4)	169 (66.3)
	Median Survival Est. (95% CI)	1.64 (1.18, 2.10)	1.64 (0.95, 2.33)
	Hazard Ratio (95% CI) [a]		1.002 (0.813, 1.235)
	Treatment P-value [b]		0.97606
	Interaction P-value [c]		0.34385
Blood and lymphatic system disorders	No. of Events (%)	28 (10.8)	60 (23.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.406 (0.259, 0.636)
	Treatment P-value [b]		0.00005
	Interaction P-value [c]		0.80489

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Table AESV.KM.S9.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Anaemia	No. of Events (%)	17 (6.6)	28 (11.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.565 (0.309, 1.033)
	Treatment P-value [b]		0.06050
	Interaction P-value [c]		0.33549
Febrile neutropenia	No. of Events (%)	4 (1.5)	15 (5.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.253 (0.084, 0.762)
	Treatment P-value [b]		0.00831
	Interaction P-value [c]		0.99066

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Table AESV.KM.S9.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Infections and infestations	No. of Events (%)	46 (17.8)	28 (11.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.627 (1.017, 2.602)
	Treatment P-value [b]		0.04092
	Interaction P-value [c]		0.60317
Neutrophil count decreased	No. of Events (%)	15 (5.8)	38 (14.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.353 (0.194, 0.642)
	Treatment P-value [b]		0.00038
	Interaction P-value [c]		0.09147

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S9.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
White blood cell count decreased	No. of Events (%)	2 (0.8)	19 (7.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.099 (0.023, 0.423)
	Treatment P-value [b]		0.00012
	Interaction P-value [c]		0.06927
Metabolism and nutrition disorders	No. of Events (%)	61 (23.6)	27 (10.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.329 (1.481, 3.665)
	Treatment P-value [b]		0.00017
	Interaction P-value [c]		0.27608

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S9.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Hyperglycaemia	No. of Events (%)	20 (7.7)	2 (0.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		10.025 (2.343, 42.893)
	Treatment P-value [b]		0.00012
	Interaction P-value [c]		0.99154
Skin and subcutaneous tissue disorders	No. of Events (%)	47 (18.1)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.98424

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Rash maculo-papular	No. of Events (%)	22 (8.5)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.99728

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table AESV.KM.S9.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Any Event	No. of Events (%)	26 (70.3)	25 (69.4)
	Median Survival Est. (95% CI)	2.27 (1.18, 5.16)	1.07 (0.26, 2.99)
	Hazard Ratio (95% CI) [a]		0.755 (0.436, 1.307)
	Treatment P-value [b]		0.36175
	Interaction P-value [c]		0.34385
Blood and lymphatic system disorders	No. of Events (%)	4 (10.8)	10 (27.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (12.94, NC)
	Hazard Ratio (95% CI) [a]		0.347 (0.109, 1.106)
	Treatment P-value [b]		0.07187
	Interaction P-value [c]		0.80489

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S9.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Anaemia	No. of Events (%)	2 (5.4)	7 (19.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (12.94, NC)
	Hazard Ratio (95% CI) [a]		0.247 (0.051, 1.190)
	Treatment P-value [b]		0.07029
	Interaction P-value [c]		0.33549
Febrile neutropenia	No. of Events (%)	0	1 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.31068
	Interaction P-value [c]		0.99066

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Infections and infestations	No. of Events (%)	6 (16.2)	5 (13.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.160 (0.354, 3.799)
	Treatment P-value [b]		0.79420
	Interaction P-value [c]		0.60317
Neutrophil count decreased	No. of Events (%)	6 (16.2)	5 (13.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.108 (0.338, 3.632)
	Treatment P-value [b]		0.88123
	Interaction P-value [c]		0.09147

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table AESV.KM.S9.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
White blood cell count decreased	No. of Events (%)	2 (5.4)	2 (5.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.948 (0.134, 6.729)
	Treatment P-value [b]		0.97162
	Interaction P-value [c]		0.06927
Metabolism and nutrition disorders	No. of Events (%)	6 (16.2)	5 (13.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.150 (0.351, 3.768)
	Treatment P-value [b]		0.79568
	Interaction P-value [c]		0.27608

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESV.KM.S9.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Hyperglycaemia	No. of Events (%)	1 (2.7)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.31731
	Interaction P-value [c]		0.99154
Skin and subcutaneous tissue disorders	No. of Events (%)	4 (10.8)	1 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.882 (0.434, 34.733)
	Treatment P-value [b]		0.18885
	Interaction P-value [c]		0.98424

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table AESV.KM.S9.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Rash maculo-papular	No. of Events (%)	0	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		NA
	Interaction P-value [c]		0.99728

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Astellas: 7465-CL-0301
Table AESV.KM.S10.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Any Event	No. of Events (%)	47 (77.0)	32 (65.3)
	Median Survival Est. (95% CI)	1.71 (0.82, 2.79)	1.68 (0.26, 4.93)
	Hazard Ratio (95% CI) [a]		1.091 (0.696, 1.710)
	Treatment P-value [b]		0.62729
	Interaction P-value [c]		0.60852
Blood and lymphatic system disorders	No. of Events (%)	5 (8.2)	12 (24.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.292 (0.103, 0.829)
	Treatment P-value [b]		0.01416
	Interaction P-value [c]		0.46482

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table AESV.KM.S10.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Anaemia	No. of Events (%)	1 (1.6)	6 (12.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.123 (0.015, 1.025)
	Treatment P-value [b]		0.02218
	Interaction P-value [c]		0.14837
Febrile neutropenia	No. of Events (%)	0	4 (8.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.02211
	Interaction P-value [c]		0.99194

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table AESV.KM.S10.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Infections and infestations	No. of Events (%)	9 (14.8)	6 (12.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.186 (0.422, 3.333)
	Treatment P-value [b]		0.76819
	Interaction P-value [c]		0.52203
Neutrophil count decreased	No. of Events (%)	5 (8.2)	7 (14.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.544 (0.173, 1.715)
	Treatment P-value [b]		0.27761
	Interaction P-value [c]		0.59524

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AESV.KM.S10.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
White blood cell count decreased	No. of Events (%)	1 (1.6)	2 (4.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.387 (0.035, 4.272)
	Treatment P-value [b]		0.42610
	Interaction P-value [c]		0.41151
Metabolism and nutrition disorders	No. of Events (%)	17 (27.9)	6 (12.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.455 (0.968, 6.227)
	Treatment P-value [b]		0.04919
	Interaction P-value [c]		0.49296

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Table AESV.KM.S10.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Hyperglycaemia	No. of Events (%)	6 (9.8)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.02565
	Interaction P-value [c]		0.98857
Skin and subcutaneous tissue disorders	No. of Events (%)	13 (21.3)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00069
	Interaction P-value [c]		0.98538

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AESV.KM.S10.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Rash maculo-papular	No. of Events (%)	1 (1.6)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.37504
	Interaction P-value [c]		0.99958

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Table AESV.KM.S10.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Any Event	No. of Events (%)	142 (70.3)	133 (65.8)
	Median Survival Est. (95% CI)	1.71 (1.18, 2.37)	1.41 (0.59, 2.33)
	Hazard Ratio (95% CI) [a]		0.955 (0.754, 1.210)
	Treatment P-value [b]		0.70435
	Interaction P-value [c]		0.60852
Blood and lymphatic system disorders	No. of Events (%)	22 (10.9)	44 (21.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.450 (0.270, 0.751)
	Treatment P-value [b]		0.00169
	Interaction P-value [c]		0.46482

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AESV.KM.S10.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Anaemia	No. of Events (%)	14 (6.9)	21 (10.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.635 (0.323, 1.249)
	Treatment P-value [b]		0.18248
	Interaction P-value [c]		0.14837
Febrile neutropenia	No. of Events (%)	3 (1.5)	10 (5.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.288 (0.079, 1.048)
	Treatment P-value [b]		0.04430
	Interaction P-value [c]		0.99194

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AESV.KM.S10.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Infections and infestations	No. of Events (%)	39 (19.3)	23 (11.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.730 (1.033, 2.896)
	Treatment P-value [b]		0.03375
	Interaction P-value [c]		0.52203
Neutrophil count decreased	No. of Events (%)	12 (5.9)	29 (14.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.380 (0.194, 0.744)
	Treatment P-value [b]		0.00374
	Interaction P-value [c]		0.59524

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

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Table AESV.KM.S10.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
White blood cell count decreased	No. of Events (%)	2 (1.0)	16 (7.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.119 (0.027, 0.518)
	Treatment P-value [b]		0.00068
	Interaction P-value [c]		0.41151
Metabolism and nutrition disorders	No. of Events (%)	40 (19.8)	24 (11.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.695 (1.022, 2.811)
	Treatment P-value [b]		0.03985
	Interaction P-value [c]		0.49296

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Analysis Plan: 15FEB2021 Confidential

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Table AESV.KM.S10.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Hyperglycaemia	No. of Events (%)	13 (6.4)	2 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.593 (1.488, 29.216)
	Treatment P-value [b]		0.00422
	Interaction P-value [c]		0.98857
Skin and subcutaneous tissue disorders	No. of Events (%)	34 (16.8)	1 (0.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		36.475 (4.993, 266.472)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.98538

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
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Table AESV.KM.S10.SAF: Time to First Severe Treatment Emergent Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Rash maculo-papular	No. of Events (%)	19 (9.4)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.99958

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
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4.6 Subgruppenanalysen zu den progressionsbereinigten schweren (CTCAE Grad ≥ 3) unerwünschten Ereignissen

Astellas: 7465-CL-0301
Table AESV.wDP.KM.S1.SAF: Time to First Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: <65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Any Event	No. of Events (%)	68 (64.2)	64 (62.1)
	Median Survival Est. (95% CI)	2.53 (1.81, 5.13)	1.61 (0.95, 4.76)
	Hazard Ratio (95% CI) [a]		0.856 (0.608, 1.204)
	Treatment P-value [b]		0.38252
	Interaction P-value [c]		0.30864

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

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Table AESV.wDP.KM.S1.SAF: Time to First Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Any Event	No. of Events (%)	138 (72.6)	125 (66.5)
	Median Survival Est. (95% CI)	1.35 (0.92, 1.87)	1.82 (0.82, 2.63)
	Hazard Ratio (95% CI) [a]		1.064 (0.835, 1.356)
	Treatment P-value [b]		0.62575
	Interaction P-value [c]		0.30864

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESV.wDP.KM.S2.SAF: Time to First Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Any Event	No. of Events (%)	164 (66.9)	150 (66.4)
	Median Survival Est. (95% CI)	1.94 (1.45, 2.83)	1.61 (1.05, 2.27)
	Hazard Ratio (95% CI) [a]		0.875 (0.701, 1.092)
	Treatment P-value [b]		0.27222
	Interaction P-value [c]		0.01282

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESV.wDP.KM.S2.SAF: Time to First Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Any Event	No. of Events (%)	42 (82.4)	39 (60.0)
	Median Survival Est. (95% CI)	0.69 (0.53, 1.77)	2.33 (0.69, NC)
	Hazard Ratio (95% CI) [a]		1.629 (1.053, 2.520)
	Treatment P-value [b]		0.03688
	Interaction P-value [c]		0.01282

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESV.wDP.KM.S3.SAF: Time to First Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Any Event	No. of Events (%)	161 (68.8)	145 (66.2)
	Median Survival Est. (95% CI)	1.81 (1.28, 2.37)	1.41 (0.95, 2.27)
	Hazard Ratio (95% CI) [a]		0.932 (0.745, 1.167)
	Treatment P-value [b]		0.55293
	Interaction P-value [c]		0.36321

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESV.wDP.KM.S3.SAF: Time to First Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Any Event	No. of Events (%)	45 (72.6)	44 (61.1)
	Median Survival Est. (95% CI)	1.74 (0.82, 3.02)	2.63 (0.82, 5.78)
	Hazard Ratio (95% CI) [a]		1.161 (0.766, 1.759)
	Treatment P-value [b]		0.41996
	Interaction P-value [c]		0.36321

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESV.wDP.KM.S4.SAF: Time to First Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Region, Level: Western Europe

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Any Event	No. of Events (%)	77 (63.1)	80 (65.0)
	Median Survival Est. (95% CI)	2.83 (1.91, 5.06)	1.71 (0.82, 3.02)
	Hazard Ratio (95% CI) [a]		0.799 (0.584, 1.092)
	Treatment P-value [b]		0.17358
	Interaction P-value [c]		0.10200

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Table AESV.wDP.KM.S4.SAF: Time to First Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Region, Level: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Any Event	No. of Events (%)	32 (76.2)	24 (61.5)
	Median Survival Est. (95% CI)	0.67 (0.46, 1.41)	2.10 (0.66, NC)
	Hazard Ratio (95% CI) [a]		1.538 (0.906, 2.613)
	Treatment P-value [b]		0.11712
	Interaction P-value [c]		0.10200

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESV.wDP.KM.S4.SAF: Time to First Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Region, Level: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Any Event	No. of Events (%)	97 (73.5)	85 (65.9)
	Median Survival Est. (95% CI)	1.43 (0.95, 2.14)	1.41 (0.59, 2.79)
	Hazard Ratio (95% CI) [a]		1.037 (0.775, 1.388)
	Treatment P-value [b]		0.76878
	Interaction P-value [c]		0.10200

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESV.wDP.KM.S5.SAF: Time to First Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Any Event	No. of Events (%)	73 (60.8)	68 (57.1)
	Median Survival Est. (95% CI)	2.53 (1.45, 5.55)	2.27 (0.99, NC)
	Hazard Ratio (95% CI) [a]		0.961 (0.691, 1.337)
	Treatment P-value [b]		0.77846
	Interaction P-value [c]		0.86124

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESV.wDP.KM.S5.SAF: Time to First Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Any Event	No. of Events (%)	133 (75.6)	121 (70.3)
	Median Survival Est. (95% CI)	1.41 (1.02, 1.94)	1.38 (0.82, 2.10)
	Hazard Ratio (95% CI) [a]		0.997 (0.779, 1.276)
	Treatment P-value [b]		0.93383
	Interaction P-value [c]		0.86124

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESV.wDP.KM.S6.SAF: Time to First Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Any Event	No. of Events (%)	66 (71.7)	54 (62.1)
	Median Survival Est. (95% CI)	0.95 (0.66, 2.33)	1.94 (0.85, 4.44)
	Hazard Ratio (95% CI) [a]		1.174 (0.819, 1.682)
	Treatment P-value [b]		0.38809
	Interaction P-value [c]		0.24754

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESV.wDP.KM.S6.SAF: Time to First Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Any Event	No. of Events (%)	140 (68.6)	135 (66.2)
	Median Survival Est. (95% CI)	1.87 (1.45, 2.79)	1.41 (0.82, 2.63)
	Hazard Ratio (95% CI) [a]		0.911 (0.719, 1.154)
	Treatment P-value [b]		0.48221
	Interaction P-value [c]		0.24754

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESV.wDP.KM.S7.SAF: Time to First Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Any Event	No. of Events (%)	100 (71.4)	57 (53.3)
	Median Survival Est. (95% CI)	1.71 (1.12, 2.73)	5.52 (2.79, NC)
	Hazard Ratio (95% CI) [a]		1.536 (1.109, 2.127)
	Treatment P-value [b]		0.00511
	Interaction P-value [c]		0.00197

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESV.wDP.KM.S7.SAF: Time to First Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Any Event	No. of Events (%)	59 (69.4)	77 (70.6)
	Median Survival Est. (95% CI)	1.18 (0.72, 2.27)	0.82 (0.30, 1.68)
	Hazard Ratio (95% CI) [a]		0.822 (0.585, 1.154)
	Treatment P-value [b]		0.24446
	Interaction P-value [c]		0.00197

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

Astellas: 7465-CL-0301
Table AESV.wDP.KM.S7.SAF: Time to First Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Any Event	No. of Events (%)	47 (66.2)	55 (73.3)
	Median Survival Est. (95% CI)	2.10 (1.28, 4.93)	0.69 (0.36, 1.71)
	Hazard Ratio (95% CI) [a]		0.655 (0.444, 0.967)
	Treatment P-value [b]		0.03446
	Interaction P-value [c]		0.00197

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

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Table AESV.wDP.KM.S8.SAF: Time to First Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Any Event	No. of Events (%)	73 (76.0)	65 (63.7)
	Median Survival Est. (95% CI)	1.25 (0.76, 2.33)	1.74 (0.82, 2.79)
	Hazard Ratio (95% CI) [a]		1.155 (0.826, 1.613)
	Treatment P-value [b]		0.39290
	Interaction P-value [c]		0.25155

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table AESV.wDP.KM.S8.SAF: Time to First Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Any Event	No. of Events (%)	133 (66.5)	124 (65.6)
	Median Survival Est. (95% CI)	1.91 (1.41, 2.83)	1.64 (0.85, 2.79)
	Hazard Ratio (95% CI) [a]		0.906 (0.709, 1.157)
	Treatment P-value [b]		0.44772
	Interaction P-value [c]		0.25155

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table AESV.wDP.KM.S9.SAF: Time to First Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Any Event	No. of Events (%)	182 (70.3)	166 (65.1)
	Median Survival Est. (95% CI)	1.64 (1.18, 2.14)	1.71 (1.22, 2.63)
	Hazard Ratio (95% CI) [a]		1.015 (0.822, 1.253)
	Treatment P-value [b]		0.88346
	Interaction P-value [c]		0.40328

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESV.wDP.KM.S9.SAF: Time to First Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Any Event	No. of Events (%)	24 (64.9)	23 (63.9)
	Median Survival Est. (95% CI)	3.55 (1.18, 5.85)	1.18 (0.26, NC)
	Hazard Ratio (95% CI) [a]		0.783 (0.442, 1.387)
	Treatment P-value [b]		0.45620
	Interaction P-value [c]		0.40328

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESV.wDP.KM.S10.SAF: Time to First Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Any Event	No. of Events (%)	46 (75.4)	30 (61.2)
	Median Survival Est. (95% CI)	1.71 (0.82, 2.79)	2.04 (0.30, NC)
	Hazard Ratio (95% CI) [a]		1.176 (0.742, 1.863)
	Treatment P-value [b]		0.44336
	Interaction P-value [c]		0.42288

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESV.wDP.KM.S10.SAF: Time to First Severe Treatment Emergent Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Any Event	No. of Events (%)	138 (68.3)	131 (64.9)
	Median Survival Est. (95% CI)	1.77 (1.18, 2.73)	1.45 (0.79, 2.37)
	Hazard Ratio (95% CI) [a]		0.951 (0.749, 1.208)
	Treatment P-value [b]		0.68517
	Interaction P-value [c]		0.42288

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 17MAY2021 17:04
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4.7 Schwerwiegende unerwünschte Ereignisse inkl. SOC und PT – Hauptebene und Subgruppenanalysen

Astellas: 7465-CL-0301
Table SAE.KM.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Any Event	No. of Events (%)	139 (47.0)	131 (45.0)
	Median Survival Est. (95% CI)	18.17 (5.45, NC)	NC (5.26, NC)
	Hazard Ratio (95% CI) [a]		0.947 (0.745, 1.205)
	Treatment P-value [b]		0.66981
	Homogeneity P-value [c]		0.05895
Blood and lymphatic system disorders	No. of Events (%)	12 (4.1)	32 (11.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.335 (0.172, 0.654)
	Treatment P-value [b]		0.00078
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.KM.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Anaemia	No. of Events (%)	4 (1.4)	6 (2.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.584 (0.162, 2.107)
	Treatment P-value [b]		0.40604
	Homogeneity P-value [c]		NA
Febrile neutropenia	No. of Events (%)	4 (1.4)	16 (5.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.234 (0.078, 0.700)
	Treatment P-value [b]		0.00464
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.KM.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Neutropenia	No. of Events (%)	4 (1.4)	8 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.506 (0.152, 1.682)
	Treatment P-value [b]		0.25704
	Homogeneity P-value [c]		NA
Cardiac disorders	No. of Events (%)	8 (2.7)	9 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.895 (0.345, 2.326)
	Treatment P-value [b]		0.82000
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.KM.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Gastrointestinal disorders	No. of Events (%)	22 (7.4)	27 (9.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.770 (0.438, 1.354)
	Treatment P-value [b]		0.36442
	Homogeneity P-value [c]		NA
Abdominal pain	No. of Events (%)	4 (1.4)	6 (2.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.636 (0.178, 2.271)
	Treatment P-value [b]		0.48187
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

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Table SAE.KM.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Diarrhoea	No. of Events (%)	7 (2.4)	4 (1.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.703 (0.498, 5.828)
	Treatment P-value [b]		0.39067
	Homogeneity P-value [c]		NA
General disorders and administration site conditions	No. of Events (%)	24 (8.1)	25 (8.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.909 (0.519, 1.592)
	Treatment P-value [b]		0.74044
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.KM.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Pyrexia	No. of Events (%)	6 (2.0)	9 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.631 (0.225, 1.776)
	Treatment P-value [b]		0.37869
	Homogeneity P-value [c]		NA
Infections and infestations	No. of Events (%)	52 (17.6)	36 (12.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.405 (0.918, 2.150)
	Treatment P-value [b]		0.11502
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

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Table SAE.KM.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Pneumonia	No. of Events (%)	12 (4.1)	8 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.438 (0.587, 3.523)
	Treatment P-value [b]		0.42412
	Homogeneity P-value [c]		NA
Urinary tract infection	No. of Events (%)	7 (2.4)	7 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.922 (0.323, 2.632)
	Treatment P-value [b]		0.87930
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

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Table SAE.KM.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Urinary tract infection bacterial	No. of Events (%)	9 (3.0)	3 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.807 (0.758, 10.401)
	Treatment P-value [b]		0.10675
	Homogeneity P-value [c]		NA
Investigations	No. of Events (%)	6 (2.0)	8 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.698 (0.242, 2.013)
	Treatment P-value [b]		0.50326
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

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Table SAE.KM.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Metabolism and nutrition disorders	No. of Events (%)	19 (6.4)	15 (5.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.219 (0.619, 2.400)
	Treatment P-value [b]		0.56690
	Homogeneity P-value [c]		NA
Musculoskeletal and connective tissue disorders	No. of Events (%)	6 (2.0)	6 (2.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.909 (0.292, 2.826)
	Treatment P-value [b]		0.86901
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

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Table SAE.KM.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	No. of Events (%)	17 (5.7)	14 (4.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.168 (0.573, 2.379)
	Treatment P-value [b]		0.66865
	Homogeneity P-value [c]		NA
Malignant neoplasm progression	No. of Events (%)	12 (4.1)	11 (3.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.062 (0.466, 2.418)
	Treatment P-value [b]		0.88597
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table SAE.KM.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Nervous system disorders	No. of Events (%)	10 (3.4)	4 (1.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.318 (0.726, 7.402)
	Treatment P-value [b]		0.14394
	Homogeneity P-value [c]		NA
Renal and urinary disorders	No. of Events (%)	28 (9.5)	16 (5.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.684 (0.909, 3.118)
	Treatment P-value [b]		0.09338
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Astellas: 7465-CL-0301
Table SAE.KM.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Acute kidney injury	No. of Events (%)	19 (6.4)	8 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.337 (1.022, 5.344)
	Treatment P-value [b]		0.03822
	Homogeneity P-value [c]		NA
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	11 (3.7)	10 (3.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.056 (0.447, 2.492)
	Treatment P-value [b]		0.90123
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Astellas: 7465-CL-0301
Table SAE.KM.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Overall, Level: NA

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=296)	Chemotherapy (N=291)
Skin and subcutaneous tissue disorders	No. of Events (%)	14 (4.7)	1 (0.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		14.228 (1.870, 108.274)
	Treatment P-value [b]		0.00072
	Homogeneity P-value [c]		NA

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.KM.S1.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: <65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Any Event	No. of Events (%)	42 (39.6)	45 (43.7)
	Median Survival Est. (95% CI)	NC (11.53, NC)	NC (3.48, NC)
	Hazard Ratio (95% CI) [a]		0.803 (0.527, 1.222)
	Treatment P-value [b]		0.33082
	Interaction P-value [c]		0.29470
Blood and lymphatic system disorders	No. of Events (%)	2 (1.9)	8 (7.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.227 (0.048, 1.070)
	Treatment P-value [b]		0.04518
	Interaction P-value [c]		0.53305

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Analysis Plan: 15FEB2021 Confidential

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Table SAE.KM.S1.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: <65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Febrile neutropenia	No. of Events (%)	0	5 (4.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.02154
	Interaction P-value [c]		0.98898
Acute kidney injury	No. of Events (%)	8 (7.5)	4 (3.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.928 (0.581, 6.403)
	Treatment P-value [b]		0.27221
	Interaction P-value [c]		0.68351

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

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Table SAE.KM.S1.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Any Event	No. of Events (%)	97 (51.1)	86 (45.7)
	Median Survival Est. (95% CI)	8.41 (4.57, NC)	NC (3.58, NC)
	Hazard Ratio (95% CI) [a]		1.055 (0.789, 1.410)
	Treatment P-value [b]		0.72012
	Interaction P-value [c]		0.29470
Blood and lymphatic system disorders	No. of Events (%)	10 (5.3)	24 (12.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.392 (0.188, 0.820)
	Treatment P-value [b]		0.00960
	Interaction P-value [c]		0.53305

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

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Table SAE.KM.S1.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Febrile neutropenia	No. of Events (%)	4 (2.1)	11 (5.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.351 (0.112, 1.103)
	Treatment P-value [b]		0.05992
	Interaction P-value [c]		0.98898
Acute kidney injury	No. of Events (%)	11 (5.8)	4 (2.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.722 (0.867, 8.552)
	Treatment P-value [b]		0.07167
	Interaction P-value [c]		0.68351

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Analysis Plan: 15FEB2021 Confidential

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Table SAE.KM.S2.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Any Event	No. of Events (%)	114 (46.5)	104 (46.0)
	Median Survival Est. (95% CI)	11.56 (5.55, NC)	NC (3.58, NC)
	Hazard Ratio (95% CI) [a]		0.909 (0.697, 1.186)
	Treatment P-value [b]		0.51142
	Interaction P-value [c]		0.36262
Blood and lymphatic system disorders	No. of Events (%)	10 (4.1)	22 (9.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.397 (0.188, 0.838)
	Treatment P-value [b]		0.01239
	Interaction P-value [c]		0.56254

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Analysis Plan: 15FEB2021 Confidential

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Table SAE.KM.S2.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Febrile neutropenia	No. of Events (%)	4 (1.6)	10 (4.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.355 (0.111, 1.132)
	Treatment P-value [b]		0.06606
	Interaction P-value [c]		0.98869
Acute kidney injury	No. of Events (%)	15 (6.1)	6 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.270 (0.881, 5.852)
	Treatment P-value [b]		0.08114
	Interaction P-value [c]		0.87019

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Analysis Plan: 15FEB2021 Confidential

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Table SAE.KM.S2.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Skin and subcutaneous tissue disorders	No. of Events (%)	11 (4.5)	1 (0.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		10.107 (1.305, 78.284)
	Treatment P-value [b]		0.00617
	Interaction P-value [c]		0.99334

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

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Table SAE.KM.S2.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Any Event	No. of Events (%)	25 (49.0)	27 (41.5)
	Median Survival Est. (95% CI)	NC (1.22, NC)	NC (4.07, NC)
	Hazard Ratio (95% CI) [a]		1.204 (0.699, 2.076)
	Treatment P-value [b]		0.51593
	Interaction P-value [c]		0.36262
Blood and lymphatic system disorders	No. of Events (%)	2 (3.9)	10 (15.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.241 (0.053, 1.098)
	Treatment P-value [b]		0.04673
	Interaction P-value [c]		0.56254

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Analysis Plan: 15FEB2021 Confidential

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Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Febrile neutropenia	No. of Events (%)	0	6 (9.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.02741
	Interaction P-value [c]		0.98869
Acute kidney injury	No. of Events (%)	4 (7.8)	2 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.670 (0.489, 14.582)
	Treatment P-value [b]		0.23226
	Interaction P-value [c]		0.87019

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table SAE.KM.S2.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Skin and subcutaneous tissue disorders	No. of Events (%)	3 (5.9)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.04648
	Interaction P-value [c]		0.99334

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

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Table SAE.KM.S3.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Any Event	No. of Events (%)	111 (47.4)	106 (48.4)
	Median Survival Est. (95% CI)	11.56 (5.26, NC)	NC (3.32, NC)
	Hazard Ratio (95% CI) [a]		0.883 (0.676, 1.152)
	Treatment P-value [b]		0.35885
	Interaction P-value [c]		0.22661
Blood and lymphatic system disorders	No. of Events (%)	9 (3.8)	27 (12.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.288 (0.135, 0.613)
	Treatment P-value [b]		0.00063
	Interaction P-value [c]		0.27726

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.KM.S3.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Febrile neutropenia	No. of Events (%)	2 (0.9)	15 (6.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.118 (0.027, 0.517)
	Treatment P-value [b]		0.00073
	Interaction P-value [c]		0.03720
Acute kidney injury	No. of Events (%)	15 (6.4)	6 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.320 (0.900, 5.983)
	Treatment P-value [b]		0.06897
	Interaction P-value [c]		0.98911

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.KM.S3.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Skin and subcutaneous tissue disorders	No. of Events (%)	12 (5.1)	1 (0.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		11.324 (1.472, 87.091)
	Treatment P-value [b]		0.00315
	Interaction P-value [c]		0.99347

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.KM.S3.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Any Event	No. of Events (%)	28 (45.2)	25 (34.7)
	Median Survival Est. (95% CI)	NC (3.55, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.280 (0.746, 2.195)
	Treatment P-value [b]		0.38647
	Interaction P-value [c]		0.22661
Blood and lymphatic system disorders	No. of Events (%)	3 (4.8)	5 (6.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.706 (0.169, 2.956)
	Treatment P-value [b]		0.65323
	Interaction P-value [c]		0.27726

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.KM.S3.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Febrile neutropenia	No. of Events (%)	2 (3.2)	1 (1.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.362 (0.214, 26.051)
	Treatment P-value [b]		0.44672
	Interaction P-value [c]		0.03720
Acute kidney injury	No. of Events (%)	4 (6.5)	2 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.352 (0.431, 12.839)
	Treatment P-value [b]		0.28953
	Interaction P-value [c]		0.98911

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

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Table SAE.KM.S3.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Skin and subcutaneous tissue disorders	No. of Events (%)	2 (3.2)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.12316
	Interaction P-value [c]		0.99347

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.KM.S4.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Western Europe

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Any Event	No. of Events (%)	59 (48.4)	66 (53.7)
	Median Survival Est. (95% CI)	8.15 (4.07, NC)	3.32 (1.45, NC)
	Hazard Ratio (95% CI) [a]		0.757 (0.533, 1.076)
	Treatment P-value [b]		0.12247
	Interaction P-value [c]		0.04866
Blood and lymphatic system disorders	No. of Events (%)	4 (3.3)	12 (9.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.311 (0.100, 0.964)
	Treatment P-value [b]		0.03293
	Interaction P-value [c]		0.92207

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

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Table SAE.KM.S4.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Western Europe

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Febrile neutropenia	No. of Events (%)	0	6 (4.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.01257
	Interaction P-value [c]		0.99987
Acute kidney injury	No. of Events (%)	9 (7.4)	3 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.917 (0.790, 10.774)
	Treatment P-value [b]		0.09400
	Interaction P-value [c]		0.81987

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

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Table SAE.KM.S4.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Any Event	No. of Events (%)	23 (54.8)	12 (30.8)
	Median Survival Est. (95% CI)	4.52 (1.48, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.007 (0.998, 4.035)
	Treatment P-value [b]		0.04107
	Interaction P-value [c]		0.04866
Blood and lymphatic system disorders	No. of Events (%)	3 (7.1)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.09112
	Interaction P-value [c]		0.92207

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

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Table SAE.KM.S4.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Febrile neutropenia	No. of Events (%)	1 (2.4)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.33523
	Interaction P-value [c]		0.99987
Acute kidney injury	No. of Events (%)	3 (7.1)	2 (5.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.431 (0.239, 8.567)
	Treatment P-value [b]		0.69943
	Interaction P-value [c]		0.81987

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Table SAE.KM.S4.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Any Event	No. of Events (%)	57 (43.2)	53 (41.1)
	Median Survival Est. (95% CI)	18.17 (8.54, NC)	NC (7.72, NC)
	Hazard Ratio (95% CI) [a]		0.989 (0.680, 1.437)
	Treatment P-value [b]		0.94549
	Interaction P-value [c]		0.04866
Blood and lymphatic system disorders	No. of Events (%)	5 (3.8)	20 (15.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.229 (0.086, 0.609)
	Treatment P-value [b]		0.00126
	Interaction P-value [c]		0.92207

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table SAE.KM.S4.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Region, Level: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Febrile neutropenia	No. of Events (%)	3 (2.3)	10 (7.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.285 (0.078, 1.034)
	Treatment P-value [b]		0.04126
	Interaction P-value [c]		0.99987
Acute kidney injury	No. of Events (%)	7 (5.3)	3 (2.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.328 (0.602, 9.007)
	Treatment P-value [b]		0.20106
	Interaction P-value [c]		0.81987

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.KM.S5.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Any Event	No. of Events (%)	49 (40.8)	39 (32.8)
	Median Survival Est. (95% CI)	18.17 (10.45, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.215 (0.798, 1.850)
	Treatment P-value [b]		0.35980
	Interaction P-value [c]		0.16209
Blood and lymphatic system disorders	No. of Events (%)	6 (5.0)	9 (7.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.664 (0.236, 1.865)
	Treatment P-value [b]		0.43574
	Interaction P-value [c]		0.12957

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

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Table SAE.KM.S5.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Febrile neutropenia	No. of Events (%)	2 (1.7)	3 (2.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.664 (0.111, 3.973)
	Treatment P-value [b]		0.65810
	Interaction P-value [c]		0.19076
Acute kidney injury	No. of Events (%)	4 (3.3)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.04479
	Interaction P-value [c]		0.98677

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Table SAE.KM.S5.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Any Event	No. of Events (%)	90 (51.1)	92 (53.5)
	Median Survival Est. (95% CI)	5.55 (3.32, NC)	3.48 (1.68, NC)
	Hazard Ratio (95% CI) [a]		0.843 (0.631, 1.128)
	Treatment P-value [b]		0.26128
	Interaction P-value [c]		0.16209
Blood and lymphatic system disorders	No. of Events (%)	6 (3.4)	23 (13.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.230 (0.094, 0.566)
	Treatment P-value [b]		0.00052
	Interaction P-value [c]		0.12957

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
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Astellas: 7465-CL-0301
Table SAE.KM.S5.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Febrile neutropenia	No. of Events (%)	2 (1.1)	13 (7.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.140 (0.032, 0.622)
	Treatment P-value [b]		0.00288
	Interaction P-value [c]		0.19076
Acute kidney injury	No. of Events (%)	15 (8.5)	8 (4.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.809 (0.767, 4.267)
	Treatment P-value [b]		0.16885
	Interaction P-value [c]		0.98677

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.KM.S6.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Any Event	No. of Events (%)	50 (54.3)	45 (51.7)
	Median Survival Est. (95% CI)	4.99 (1.84, NC)	3.32 (1.45, NC)
	Hazard Ratio (95% CI) [a]		0.944 (0.631, 1.413)
	Treatment P-value [b]		0.81058
	Interaction P-value [c]		0.93886
Blood and lymphatic system disorders	No. of Events (%)	5 (5.4)	13 (14.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.336 (0.120, 0.943)
	Treatment P-value [b]		0.03085
	Interaction P-value [c]		0.94887

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Analysis Plan: 15FEB2021 Confidential

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Table SAE.KM.S6.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Febrile neutropenia	No. of Events (%)	2 (2.2)	6 (6.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.305 (0.062, 1.514)
	Treatment P-value [b]		0.13327
	Interaction P-value [c]		0.68061
Acute kidney injury	No. of Events (%)	5 (5.4)	3 (3.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.587 (0.379, 6.642)
	Treatment P-value [b]		0.58241
	Interaction P-value [c]		0.53192

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

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Table SAE.KM.S6.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Any Event	No. of Events (%)	89 (43.6)	86 (42.2)
	Median Survival Est. (95% CI)	18.17 (8.41, NC)	NC (7.72, NC)
	Hazard Ratio (95% CI) [a]		0.963 (0.716, 1.295)
	Treatment P-value [b]		0.83745
	Interaction P-value [c]		0.93886
Blood and lymphatic system disorders	No. of Events (%)	7 (3.4)	19 (9.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.351 (0.148, 0.835)
	Treatment P-value [b]		0.01327
	Interaction P-value [c]		0.94887

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

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Table SAE.KM.S6.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Febrile neutropenia	No. of Events (%)	2 (1.0)	10 (4.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.192 (0.042, 0.877)
	Treatment P-value [b]		0.01712
	Interaction P-value [c]		0.68061
Acute kidney injury	No. of Events (%)	14 (6.9)	5 (2.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.780 (1.001, 7.718)
	Treatment P-value [b]		0.03886
	Interaction P-value [c]		0.53192

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.KM.S7.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Any Event	No. of Events (%)	67 (47.9)	35 (32.7)
	Median Survival Est. (95% CI)	10.45 (4.83, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.533 (1.019, 2.307)
	Treatment P-value [b]		0.03005
	Interaction P-value [c]		0.01489
Blood and lymphatic system disorders	No. of Events (%)	5 (3.6)	6 (5.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.625 (0.191, 2.047)
	Treatment P-value [b]		0.40839
	Interaction P-value [c]		0.58265

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

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Table SAE.KM.S7.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Acute kidney injury	No. of Events (%)	11 (7.9)	2 (1.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.210 (0.933, 18.993)
	Treatment P-value [b]		0.04049
	Interaction P-value [c]		0.37645

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

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Table SAE.KM.S7.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Any Event	No. of Events (%)	37 (43.5)	51 (46.8)
	Median Survival Est. (95% CI)	18.17 (5.09, NC)	NC (1.68, NC)
	Hazard Ratio (95% CI) [a]		0.819 (0.536, 1.250)
	Treatment P-value [b]		0.36545
	Interaction P-value [c]		0.01489
Blood and lymphatic system disorders	No. of Events (%)	4 (4.7)	15 (13.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.318 (0.106, 0.960)
	Treatment P-value [b]		0.03459
	Interaction P-value [c]		0.58265

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

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Table SAE.KM.S7.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Acute kidney injury	No. of Events (%)	3 (3.5)	4 (3.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.953 (0.213, 4.261)
	Treatment P-value [b]		0.95885
	Interaction P-value [c]		0.37645

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.KM.S7.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Any Event	No. of Events (%)	35 (49.3)	45 (60.0)
	Median Survival Est. (95% CI)	11.53 (1.84, NC)	1.94 (0.56, 6.60)
	Hazard Ratio (95% CI) [a]		0.657 (0.422, 1.022)
	Treatment P-value [b]		0.06146
	Interaction P-value [c]		0.01489
Blood and lymphatic system disorders	No. of Events (%)	3 (4.2)	11 (14.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.265 (0.074, 0.949)
	Treatment P-value [b]		0.02917
	Interaction P-value [c]		0.58265

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Analysis Plan: 15FEB2021 Confidential

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Table SAE.KM.S7.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Acute kidney injury	No. of Events (%)	5 (7.0)	2 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.624 (0.509, 13.526)
	Treatment P-value [b]		0.24005
	Interaction P-value [c]		0.37645

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

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Table SAE.KM.S8.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Any Event	No. of Events (%)	42 (43.8)	38 (37.3)
	Median Survival Est. (95% CI)	11.56 (8.15, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.087 (0.701, 1.686)
	Treatment P-value [b]		0.69976
	Interaction P-value [c]		0.49526
Blood and lymphatic system disorders	No. of Events (%)	6 (6.3)	13 (12.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.466 (0.177, 1.227)
	Treatment P-value [b]		0.11477
	Interaction P-value [c]		0.45872

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table SAE.KM.S8.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Febrile neutropenia	No. of Events (%)	3 (3.1)	7 (6.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.440 (0.114, 1.703)
	Treatment P-value [b]		0.22070
	Interaction P-value [c]		0.24274
Acute kidney injury	No. of Events (%)	5 (5.2)	2 (2.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.661 (0.516, 13.714)
	Treatment P-value [b]		0.23106
	Interaction P-value [c]		0.84247

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table SAE.KM.S8.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Skin and subcutaneous tissue disorders	No. of Events (%)	4 (4.2)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.03907
	Interaction P-value [c]		0.99198

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table SAE.KM.S8.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Any Event	No. of Events (%)	97 (48.5)	93 (49.2)
	Median Survival Est. (95% CI)	18.17 (4.07, NC)	7.72 (3.09, NC)
	Hazard Ratio (95% CI) [a]		0.906 (0.682, 1.205)
	Treatment P-value [b]		0.50177
	Interaction P-value [c]		0.49526
Blood and lymphatic system disorders	No. of Events (%)	6 (3.0)	19 (10.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.282 (0.112, 0.705)
	Treatment P-value [b]		0.00389
	Interaction P-value [c]		0.45872

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Astellas: 7465-CL-0301
Table SAE.KM.S8.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Febrile neutropenia	No. of Events (%)	1 (0.5)	9 (4.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.101 (0.013, 0.798)
	Treatment P-value [b]		0.00754
	Interaction P-value [c]		0.24274
Acute kidney injury	No. of Events (%)	14 (7.0)	6 (3.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.195 (0.843, 5.713)
	Treatment P-value [b]		0.09426
	Interaction P-value [c]		0.84247

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table SAE.KM.S8.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Skin and subcutaneous tissue disorders	No. of Events (%)	10 (5.0)	1 (0.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.569 (1.225, 74.754)
	Treatment P-value [b]		0.00845
	Interaction P-value [c]		0.99198

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table SAE.KM.S9.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Any Event	No. of Events (%)	121 (46.7)	114 (44.7)
	Median Survival Est. (95% CI)	11.56 (5.26, NC)	NC (5.91, NC)
	Hazard Ratio (95% CI) [a]		0.971 (0.752, 1.255)
	Treatment P-value [b]		0.82577
	Interaction P-value [c]		0.83910
Blood and lymphatic system disorders	No. of Events (%)	11 (4.2)	30 (11.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.340 (0.170, 0.678)
	Treatment P-value [b]		0.00132
	Interaction P-value [c]		0.79331

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table SAE.KM.S9.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Febrile neutropenia	No. of Events (%)	4 (1.5)	15 (5.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.253 (0.084, 0.762)
	Treatment P-value [b]		0.00831
	Interaction P-value [c]		0.99066
Acute kidney injury	No. of Events (%)	18 (6.9)	7 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.517 (1.051, 6.029)
	Treatment P-value [b]		0.03205
	Interaction P-value [c]		0.53118

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Analysis Plan: 15FEB2021 Confidential

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Table SAE.KM.S9.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Skin and subcutaneous tissue disorders	No. of Events (%)	11 (4.2)	1 (0.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		10.944 (1.413, 84.773)
	Treatment P-value [b]		0.00406
	Interaction P-value [c]		0.99293

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

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Table SAE.KM.S9.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Any Event	No. of Events (%)	18 (48.6)	17 (47.2)
	Median Survival Est. (95% CI)	18.17 (3.71, NC)	NC (1.35, NC)
	Hazard Ratio (95% CI) [a]		0.903 (0.465, 1.752)
	Treatment P-value [b]		0.76216
	Interaction P-value [c]		0.83910
Blood and lymphatic system disorders	No. of Events (%)	1 (2.7)	2 (5.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.475 (0.043, 5.232)
	Treatment P-value [b]		0.54730
	Interaction P-value [c]		0.79331

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Table SAE.KM.S9.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Febrile neutropenia	No. of Events (%)	0	1 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.31068
	Interaction P-value [c]		0.99066
Acute kidney injury	No. of Events (%)	1 (2.7)	1 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.995 (0.062, 15.903)
	Treatment P-value [b]		0.99227
	Interaction P-value [c]		0.53118

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table SAE.KM.S9.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Skin and subcutaneous tissue disorders	No. of Events (%)	3 (8.1)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.08515
	Interaction P-value [c]		0.99293

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table SAE.KM.S10.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Any Event	No. of Events (%)	27 (44.3)	25 (51.0)
	Median Survival Est. (95% CI)	NC (4.60, NC)	7.72 (1.41, NC)
	Hazard Ratio (95% CI) [a]		0.748 (0.434, 1.289)
	Treatment P-value [b]		0.31256
	Interaction P-value [c]		0.18150
Blood and lymphatic system disorders	No. of Events (%)	3 (4.9)	6 (12.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.378 (0.094, 1.510)
	Treatment P-value [b]		0.15293
	Interaction P-value [c]		0.77814

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table SAE.KM.S10.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Febrile neutropenia	No. of Events (%)	0	4 (8.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.02211
	Interaction P-value [c]		0.99194
Acute kidney injury	No. of Events (%)	4 (6.6)	1 (2.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.188 (0.356, 28.517)
	Treatment P-value [b]		0.27331
	Interaction P-value [c]		0.74936

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table SAE.KM.S10.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Skin and subcutaneous tissue disorders	No. of Events (%)	3 (4.9)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.12309
	Interaction P-value [c]		0.99087

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table SAE.KM.S10.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Any Event	No. of Events (%)	98 (48.5)	83 (41.1)
	Median Survival Est. (95% CI)	11.53 (4.83, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.140 (0.851, 1.527)
	Treatment P-value [b]		0.38046
	Interaction P-value [c]		0.18150
Blood and lymphatic system disorders	No. of Events (%)	8 (4.0)	16 (7.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.477 (0.204, 1.114)
	Treatment P-value [b]		0.08031
	Interaction P-value [c]		0.77814

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table SAE.KM.S10.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Febrile neutropenia	No. of Events (%)	3 (1.5)	10 (5.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.288 (0.079, 1.048)
	Treatment P-value [b]		0.04430
	Interaction P-value [c]		0.99194
Acute kidney injury	No. of Events (%)	13 (6.4)	6 (3.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.157 (0.820, 5.677)
	Treatment P-value [b]		0.11417
	Interaction P-value [c]		0.74936

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.KM.S10.SAF: Time to First Treatment Emergent Serious Adverse Event (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Skin and subcutaneous tissue disorders	No. of Events (%)	11 (5.4)	1 (0.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		11.215 (1.448, 86.867)
	Treatment P-value [b]		0.00349
	Interaction P-value [c]		0.99087

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
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4.8 Subgruppenanalysen zu den progressionsbereinigten schwerwiegenden unerwünschten Ereignissen

Astellas: 7465-CL-0301
Table SAE.wDP.KM.S1.SAF: Time to First Treatment Emergent Serious Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: <65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Any Event	No. of Events (%)	40 (37.7)	42 (40.8)
	Median Survival Est. (95% CI)	NC (11.53, NC)	NC (4.47, NC)
	Hazard Ratio (95% CI) [a]		0.816 (0.529, 1.259)
	Treatment P-value [b]		0.38851
	Interaction P-value [c]		0.36747

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.wDP.KM.S1.SAF: Time to First Treatment Emergent Serious Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Any Event	No. of Events (%)	91 (47.9)	82 (43.6)
	Median Survival Est. (95% CI)	10.45 (4.83, NC)	NC (4.44, NC)
	Hazard Ratio (95% CI) [a]		1.040 (0.771, 1.401)
	Treatment P-value [b]		0.80439
	Interaction P-value [c]		0.36747

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.wDP.KM.S2.SAF: Time to First Treatment Emergent Serious Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Any Event	No. of Events (%)	106 (43.3)	99 (43.8)
	Median Survival Est. (95% CI)	18.17 (8.54, NC)	NC (4.47, NC)
	Hazard Ratio (95% CI) [a]		0.890 (0.676, 1.170)
	Treatment P-value [b]		0.42454
	Interaction P-value [c]		0.23703

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.wDP.KM.S2.SAF: Time to First Treatment Emergent Serious Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Any Event	No. of Events (%)	25 (49.0)	25 (38.5)
	Median Survival Est. (95% CI)	NC (1.45, NC)	NC (4.07, NC)
	Hazard Ratio (95% CI) [a]		1.292 (0.742, 2.250)
	Treatment P-value [b]		0.37760
	Interaction P-value [c]		0.23703

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.wDP.KM.S3.SAF: Time to First Treatment Emergent Serious Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Any Event	No. of Events (%)	104 (44.4)	99 (45.2)
	Median Survival Est. (95% CI)	18.17 (8.15, NC)	NC (4.44, NC)
	Hazard Ratio (95% CI) [a]		0.886 (0.672, 1.167)
	Treatment P-value [b]		0.38861
	Interaction P-value [c]		0.29146

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.wDP.KM.S3.SAF: Time to First Treatment Emergent Serious Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Any Event	No. of Events (%)	27 (43.5)	25 (34.7)
	Median Survival Est. (95% CI)	NC (3.71, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.230 (0.714, 2.120)
	Treatment P-value [b]		0.46867
	Interaction P-value [c]		0.29146

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.wDP.KM.S4.SAF: Time to First Treatment Emergent Serious Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Region, Level: Western Europe

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Any Event	No. of Events (%)	54 (44.3)	62 (50.4)
	Median Survival Est. (95% CI)	NC (4.83, NC)	3.48 (2.10, NC)
	Hazard Ratio (95% CI) [a]		0.740 (0.514, 1.066)
	Treatment P-value [b]		0.10398
	Interaction P-value [c]		0.02846

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.wDP.KM.S4.SAF: Time to First Treatment Emergent Serious Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Region, Level: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Any Event	No. of Events (%)	23 (54.8)	11 (28.2)
	Median Survival Est. (95% CI)	4.52 (1.48, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.212 (1.078, 4.539)
	Treatment P-value [b]		0.02350
	Interaction P-value [c]		0.02846

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.wDP.KM.S4.SAF: Time to First Treatment Emergent Serious Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Region, Level: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Any Event	No. of Events (%)	54 (40.9)	51 (39.5)
	Median Survival Est. (95% CI)	18.17 (10.45, NC)	NC (7.72, NC)
	Hazard Ratio (95% CI) [a]		0.968 (0.660, 1.420)
	Treatment P-value [b]		0.86051
	Interaction P-value [c]		0.02846

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.wDP.KM.S5.SAF: Time to First Treatment Emergent Serious Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Any Event	No. of Events (%)	46 (38.3)	38 (31.9)
	Median Survival Est. (95% CI)	18.17 (18.17, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.164 (0.757, 1.789)
	Treatment P-value [b]		0.48484
	Interaction P-value [c]		0.24926

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.wDP.KM.S5.SAF: Time to First Treatment Emergent Serious Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Any Event	No. of Events (%)	85 (48.3)	86 (50.0)
	Median Survival Est. (95% CI)	11.53 (3.55, NC)	5.26 (2.10, NC)
	Hazard Ratio (95% CI) [a]		0.855 (0.634, 1.155)
	Treatment P-value [b]		0.32168
	Interaction P-value [c]		0.24926

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.wDP.KM.S6.SAF: Time to First Treatment Emergent Serious Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Any Event	No. of Events (%)	45 (48.9)	42 (48.3)
	Median Survival Est. (95% CI)	11.53 (2.14, NC)	NC (1.45, NC)
	Hazard Ratio (95% CI) [a]		0.902 (0.592, 1.374)
	Treatment P-value [b]		0.66627
	Interaction P-value [c]		0.75773

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.wDP.KM.S6.SAF: Time to First Treatment Emergent Serious Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Any Event	No. of Events (%)	86 (42.2)	82 (40.2)
	Median Survival Est. (95% CI)	18.17 (8.54, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.979 (0.723, 1.325)
	Treatment P-value [b]		0.91334
	Interaction P-value [c]		0.75773

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.wDP.KM.S7.SAF: Time to First Treatment Emergent Serious Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Any Event	No. of Events (%)	65 (46.4)	31 (29.0)
	Median Survival Est. (95% CI)	10.45 (4.99, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.673 (1.091, 2.567)
	Treatment P-value [b]		0.01326
	Interaction P-value [c]		0.00371

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.wDP.KM.S7.SAF: Time to First Treatment Emergent Serious Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Any Event	No. of Events (%)	35 (41.2)	49 (45.0)
	Median Survival Est. (95% CI)	18.17 (5.09, NC)	NC (2.63, NC)
	Hazard Ratio (95% CI) [a]		0.808 (0.524, 1.247)
	Treatment P-value [b]		0.33768
	Interaction P-value [c]		0.00371

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table SAE.wDP.KM.S7.SAF: Time to First Treatment Emergent Serious Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Any Event	No. of Events (%)	31 (43.7)	44 (58.7)
	Median Survival Est. (95% CI)	NC (3.55, NC)	2.27 (0.79, NC)
	Hazard Ratio (95% CI) [a]		0.597 (0.377, 0.945)
	Treatment P-value [b]		0.02806
	Interaction P-value [c]		0.00371

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.wDP.KM.S8.SAF: Time to First Treatment Emergent Serious Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Any Event	No. of Events (%)	39 (40.6)	37 (36.3)
	Median Survival Est. (95% CI)	NC (8.54, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.026 (0.654, 1.608)
	Treatment P-value [b]		0.89577
	Interaction P-value [c]		0.70425

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.wDP.KM.S8.SAF: Time to First Treatment Emergent Serious Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Any Event	No. of Events (%)	92 (46.0)	87 (46.0)
	Median Survival Est. (95% CI)	18.17 (4.83, NC)	NC (3.81, NC)
	Hazard Ratio (95% CI) [a]		0.924 (0.689, 1.239)
	Treatment P-value [b]		0.60074
	Interaction P-value [c]		0.70425

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.wDP.KM.S9.SAF: Time to First Treatment Emergent Serious Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Any Event	No. of Events (%)	114 (44.0)	108 (42.4)
	Median Survival Est. (95% CI)	NC (8.41, NC)	NC (7.72, NC)
	Hazard Ratio (95% CI) [a]		0.967 (0.744, 1.259)
	Treatment P-value [b]		0.80638
	Interaction P-value [c]		0.83732

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.wDP.KM.S9.SAF: Time to First Treatment Emergent Serious Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Any Event	No. of Events (%)	17 (45.9)	16 (44.4)
	Median Survival Est. (95% CI)	18.17 (3.71, NC)	NC (1.35, NC)
	Hazard Ratio (95% CI) [a]		0.896 (0.453, 1.774)
	Treatment P-value [b]		0.76039
	Interaction P-value [c]		0.83732

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.wDP.KM.S10.SAF: Time to First Treatment Emergent Serious Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Any Event	No. of Events (%)	26 (42.6)	23 (46.9)
	Median Survival Est. (95% CI)	NC (4.60, NC)	NC (1.41, NC)
	Hazard Ratio (95% CI) [a]		0.782 (0.446, 1.371)
	Treatment P-value [b]		0.41636
	Interaction P-value [c]		0.26198

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAE.wDP.KM.S10.SAF: Time to First Treatment Emergent Serious Adverse Event Excluding Those Related to Disease Progression (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Any Event	No. of Events (%)	93 (46.0)	80 (39.6)
	Median Survival Est. (95% CI)	18.17 (5.26, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.126 (0.835, 1.518)
	Treatment P-value [b]		0.43697
	Interaction P-value [c]		0.26198

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

4.9 Subgruppenanalysen zu den Abbrüchen der Studienmedikation aufgrund von unerwünschten Ereignissen

Astellas: 7465-CL-0301
Table AED.KM.S1.SAF: Time to First TEAE Leading to Study Drug Discontinuation (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: <65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Any Event	No. of Events (%)	15 (14.2)	19 (18.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.694 (0.353, 1.367)
	Treatment P-value [b]		0.30974
	Interaction P-value [c]		0.38477

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AED.KM.S1.SAF: Time to First TEAE Leading to Study Drug Discontinuation (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Any Event	No. of Events (%)	39 (20.5)	37 (19.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.996 (0.635, 1.561)
	Treatment P-value [b]		0.99751
	Interaction P-value [c]		0.38477

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AED.KM.S2.SAF: Time to First TEAE Leading to Study Drug Discontinuation (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: <75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Any Event	No. of Events (%)	40 (16.3)	43 (19.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.792 (0.515, 1.219)
	Treatment P-value [b]		0.28020
	Interaction P-value [c]		0.22225

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AED.KM.S2.SAF: Time to First TEAE Leading to Study Drug Discontinuation (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Any Event	No. of Events (%)	14 (27.5)	13 (20.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.361 (0.640, 2.897)
	Treatment P-value [b]		0.39340
	Interaction P-value [c]		0.22225

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

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Table AED.KM.S3.SAF: Time to First TEAE Leading to Study Drug Discontinuation (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Any Event	No. of Events (%)	46 (19.7)	42 (19.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.945 (0.622, 1.436)
	Treatment P-value [b]		0.79683
	Interaction P-value [c]		0.45511

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

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Table AED.KM.S3.SAF: Time to First TEAE Leading to Study Drug Discontinuation (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Any Event	No. of Events (%)	8 (12.9)	14 (19.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.654 (0.274, 1.560)
	Treatment P-value [b]		0.32997
	Interaction P-value [c]		0.45511

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

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Table AED.KM.S4.SAF: Time to First TEAE Leading to Study Drug Discontinuation (Months) (Safety Analysis Set)
Subgroup: Region, Level: Western Europe

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Any Event	No. of Events (%)	28 (23.0)	28 (22.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.921 (0.545, 1.555)
	Treatment P-value [b]		0.75806
	Interaction P-value [c]		0.05435

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AED.KM.S4.SAF: Time to First TEAE Leading to Study Drug Discontinuation (Months) (Safety Analysis Set)
Subgroup: Region, Level: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Any Event	No. of Events (%)	8 (19.0)	1 (2.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.901 (0.988, 63.169)
	Treatment P-value [b]		0.02255
	Interaction P-value [c]		0.05435

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

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Table AED.KM.S4.SAF: Time to First TEAE Leading to Study Drug Discontinuation (Months) (Safety Analysis Set)
Subgroup: Region, Level: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Any Event	No. of Events (%)	18 (13.6)	27 (20.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.598 (0.329, 1.086)
	Treatment P-value [b]		0.08359
	Interaction P-value [c]		0.05435

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

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Table AED.KM.S5.SAF: Time to First TEAE Leading to Study Drug Discontinuation (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Any Event	No. of Events (%)	24 (20.0)	20 (16.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.168 (0.645, 2.115)
	Treatment P-value [b]		0.60651
	Interaction P-value [c]		0.23605

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AED.KM.S5.SAF: Time to First TEAE Leading to Study Drug Discontinuation (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Any Event	No. of Events (%)	30 (17.0)	36 (20.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.735 (0.453, 1.194)
	Treatment P-value [b]		0.22437
	Interaction P-value [c]		0.23605

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table AED.KM.S6.SAF: Time to First TEAE Leading to Study Drug Discontinuation (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Any Event	No. of Events (%)	25 (27.2)	16 (18.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.403 (0.748, 2.630)
	Treatment P-value [b]		0.25033
	Interaction P-value [c]		0.06854

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AED.KM.S6.SAF: Time to First TEAE Leading to Study Drug Discontinuation (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Any Event	No. of Events (%)	29 (14.2)	40 (19.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.674 (0.418, 1.087)
	Treatment P-value [b]		0.10958
	Interaction P-value [c]		0.06854

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table AED.KM.S7.SAF: Time to First TEAE Leading to Study Drug Discontinuation (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Any Event	No. of Events (%)	17 (12.1)	17 (15.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.705 (0.360, 1.381)
	Treatment P-value [b]		0.27540
	Interaction P-value [c]		0.53090

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table AED.KM.S7.SAF: Time to First TEAE Leading to Study Drug Discontinuation (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Any Event	No. of Events (%)	15 (17.6)	20 (18.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.902 (0.462, 1.762)
	Treatment P-value [b]		0.81116
	Interaction P-value [c]		0.53090

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table AED.KM.S7.SAF: Time to First TEAE Leading to Study Drug Discontinuation (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Any Event	No. of Events (%)	22 (31.0)	19 (25.3)
	Median Survival Est. (95% CI)	NC (11.53, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.187 (0.643, 2.193)
	Treatment P-value [b]		0.57501
	Interaction P-value [c]		0.53090

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
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Astellas: 7465-CL-0301
Table AED.KM.S8.SAF: Time to First TEAE Leading to Study Drug Discontinuation (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Any Event	No. of Events (%)	19 (19.8)	20 (19.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.962 (0.513, 1.802)
	Treatment P-value [b]		0.89574
	Interaction P-value [c]		0.76290

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AED.KM.S8.SAF: Time to First TEAE Leading to Study Drug Discontinuation (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Any Event	No. of Events (%)	35 (17.5)	36 (19.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.853 (0.535, 1.358)
	Treatment P-value [b]		0.50923
	Interaction P-value [c]		0.76290

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table AED.KM.S9.SAF: Time to First TEAE Leading to Study Drug Discontinuation (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Any Event	No. of Events (%)	47 (18.1)	49 (19.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.887 (0.594, 1.323)
	Treatment P-value [b]		0.55831
	Interaction P-value [c]		0.98862

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:50
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AED.KM.S9.SAF: Time to First TEAE Leading to Study Drug Discontinuation (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Any Event	No. of Events (%)	7 (18.9)	7 (19.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.894 (0.314, 2.549)
	Treatment P-value [b]		0.79432
	Interaction P-value [c]		0.98862

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AED.KM.S10.SAF: Time to First TEAE Leading to Study Drug Discontinuation (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Any Event	No. of Events (%)	11 (18.0)	9 (18.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.948 (0.393, 2.287)
	Treatment P-value [b]		0.92225
	Interaction P-value [c]		0.99418

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AED.KM.S10.SAF: Time to First TEAE Leading to Study Drug Discontinuation (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Any Event	No. of Events (%)	37 (18.3)	37 (18.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.944 (0.598, 1.489)
	Treatment P-value [b]		0.81198
	Interaction P-value [c]		0.99418

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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4.10 Subgruppenanalysen zu den unerwünschten Ereignissen von besonderem Interesse

4.10.1 Gesamtrate

Astellas: 7465-CL-0301
Table AESI.KM.S1.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Hyperglycemia	No. of Events (%)	8 (7.5)	2 (1.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.849 (0.818, 18.119)
	Treatment P-value [b]		0.06744
	Interaction P-value [c]		0.81807

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESI.KM.S1.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Infusion related reaction	No. of Events (%)	8 (7.5)	6 (5.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.259 (0.437, 3.630)
	Treatment P-value [b]		0.65250
	Interaction P-value [c]		0.62786
Neuropathy	No. of Events (%)	52 (49.1)	36 (35.0)
	Median Survival Est. (95% CI)	6.93 (5.13, NC)	NC (9.07, NC)
	Hazard Ratio (95% CI) [a]		1.298 (0.849, 1.986)
	Treatment P-value [b]		0.21042
	Interaction P-value [c]		0.53737

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

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Table AESI.KM.S1.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Ocular disorders	No. of Events (%)	20 (18.9)	7 (6.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.839 (1.200, 6.713)
	Treatment P-value [b]		0.01232
	Interaction P-value [c]		0.37492
Skin reactions	No. of Events (%)	54 (50.9)	21 (20.4)
	Median Survival Est. (95% CI)	6.60 (1.35, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.151 (1.903, 5.218)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.79383

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESI.KM.S1.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Hyperglycemia	No. of Events (%)	27 (14.2)	6 (3.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.746 (1.959, 11.496)
	Treatment P-value [b]		0.00015
	Interaction P-value [c]		0.81807

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AESI.KM.S1.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Infusion related reaction	No. of Events (%)	19 (10.0)	11 (5.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.734 (0.825, 3.644)
	Treatment P-value [b]		0.14394
	Interaction P-value [c]		0.62786
Neuropathy	No. of Events (%)	97 (51.1)	64 (34.0)
	Median Survival Est. (95% CI)	4.86 (4.04, 7.92)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.534 (1.118, 2.104)
	Treatment P-value [b]		0.00837
	Interaction P-value [c]		0.53737

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AESI.KM.S1.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Ocular disorders	No. of Events (%)	63 (33.2)	16 (8.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.507 (2.603, 7.803)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.37492
Skin reactions	No. of Events (%)	109 (57.4)	41 (21.8)
	Median Survival Est. (95% CI)	2.33 (1.05, 5.98)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.422 (2.388, 4.904)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.79383

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

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Table AESI.KM.S2.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Hyperglycemia	No. of Events (%)	25 (10.2)	6 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.912 (1.605, 9.535)
	Treatment P-value [b]		0.00120
	Interaction P-value [c]		0.49979

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

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Table AESI.KM.S2.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Infusion related reaction	No. of Events (%)	27 (11.0)	10 (4.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.501 (1.210, 5.167)
	Treatment P-value [b]		0.01038
	Interaction P-value [c]		0.98650
Neuropathy	No. of Events (%)	126 (51.4)	78 (34.5)
	Median Survival Est. (95% CI)	5.55 (4.60, 8.31)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.452 (1.095, 1.926)
	Treatment P-value [b]		0.00852
	Interaction P-value [c]		0.82323

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AESI.KM.S2.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Ocular disorders	No. of Events (%)	63 (25.7)	16 (7.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.900 (2.253, 6.751)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.75310
Skin reactions	No. of Events (%)	136 (55.5)	49 (21.7)
	Median Survival Est. (95% CI)	3.35 (1.35, 7.49)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.300 (2.379, 4.577)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.97845

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

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Table AESI.KM.S2.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Hyperglycemia	No. of Events (%)	10 (19.6)	2 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.171 (1.571, 32.735)
	Treatment P-value [b]		0.00339
	Interaction P-value [c]		0.49979

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESI.KM.S2.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Infusion related reaction	No. of Events (%)	0	7 (10.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.01927
	Interaction P-value [c]		0.98650
Neuropathy	No. of Events (%)	23 (45.1)	22 (33.8)
	Median Survival Est. (95% CI)	7.92 (3.68, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.348 (0.752, 2.420)
	Treatment P-value [b]		0.32947
	Interaction P-value [c]		0.82323

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Table AESI.KM.S2.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Ocular disorders	No. of Events (%)	20 (39.2)	7 (10.8)
	Median Survival Est. (95% CI)	NC (3.94, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.594 (1.942, 10.871)
	Treatment P-value [b]		0.00020
	Interaction P-value [c]		0.75310
Skin reactions	No. of Events (%)	27 (52.9)	13 (20.0)
	Median Survival Est. (95% CI)	2.79 (0.56, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.334 (1.719, 6.464)
	Treatment P-value [b]		0.00018
	Interaction P-value [c]		0.97845

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESI.KM.S3.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Hyperglycemia	No. of Events (%)	32 (13.7)	6 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.161 (2.158, 12.345)
	Treatment P-value [b]		0.00004
	Interaction P-value [c]		0.30360

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Astellas: 7465-CL-0301
Table AESI.KM.S3.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Infusion related reaction	No. of Events (%)	19 (8.1)	13 (5.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.345 (0.664, 2.724)
	Treatment P-value [b]		0.40965
	Interaction P-value [c]		0.40016
Neuropathy	No. of Events (%)	123 (52.6)	72 (32.9)
	Median Survival Est. (95% CI)	5.13 (4.21, 8.31)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.612 (1.205, 2.157)
	Treatment P-value [b]		0.00108
	Interaction P-value [c]		0.10911

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESI.KM.S3.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Ocular disorders	No. of Events (%)	69 (29.5)	17 (7.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.153 (2.442, 7.062)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.58783
Skin reactions	No. of Events (%)	131 (56.0)	42 (19.2)
	Median Survival Est. (95% CI)	2.79 (1.05, 7.06)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.838 (2.709, 5.437)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.10151

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESI.KM.S3.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Hyperglycemia	No. of Events (%)	3 (4.8)	2 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.816 (0.303, 10.866)
	Treatment P-value [b]		0.50099
	Interaction P-value [c]		0.30360

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESI.KM.S3.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Infusion related reaction	No. of Events (%)	8 (12.9)	4 (5.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.445 (0.736, 8.120)
	Treatment P-value [b]		0.13643
	Interaction P-value [c]		0.40016
Neuropathy	No. of Events (%)	26 (41.9)	28 (38.9)
	Median Survival Est. (95% CI)	NC (4.63, NC)	NC (5.26, NC)
	Hazard Ratio (95% CI) [a]		0.981 (0.575, 1.673)
	Treatment P-value [b]		0.97073
	Interaction P-value [c]		0.10911

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AESI.KM.S3.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Ocular disorders	No. of Events (%)	14 (22.6)	6 (8.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.069 (1.179, 7.987)
	Treatment P-value [b]		0.01470
	Interaction P-value [c]		0.58783
Skin reactions	No. of Events (%)	32 (51.6)	20 (27.8)
	Median Survival Est. (95% CI)	6.60 (1.31, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.215 (1.266, 3.874)
	Treatment P-value [b]		0.00423
	Interaction P-value [c]		0.10151

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

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Table AESI.KM.S4.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Region, Level: Western Europe

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Hyperglycemia	No. of Events (%)	16 (13.1)	5 (4.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.211 (1.176, 8.764)
	Treatment P-value [b]		0.01544
	Interaction P-value [c]		0.98231

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AESI.KM.S4.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Region, Level: Western Europe

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Infusion related reaction	No. of Events (%)	5 (4.1)	7 (5.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.680 (0.216, 2.143)
	Treatment P-value [b]		0.52819
	Interaction P-value [c]		0.18780
Neuropathy	No. of Events (%)	61 (50.0)	30 (24.4)
	Median Survival Est. (95% CI)	6.21 (3.29, 11.99)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.279 (1.471, 3.530)
	Treatment P-value [b]		0.00018
	Interaction P-value [c]		0.02171

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AESI.KM.S4.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Region, Level: Western Europe

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Ocular disorders	No. of Events (%)	48 (39.3)	5 (4.1)
	Median Survival Est. (95% CI)	NC (6.77, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		11.601 (4.616, 29.153)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.00371
Skin reactions	No. of Events (%)	55 (45.1)	16 (13.0)
	Median Survival Est. (95% CI)	11.86 (3.78, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.969 (2.274, 6.926)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.75820

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESI.KM.S4.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Region, Level: US

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Hyperglycemia	No. of Events (%)	8 (19.0)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00421
	Interaction P-value [c]		0.98231

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
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Table AESI.KM.S4.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Region, Level: US

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Infusion related reaction	No. of Events (%)	5 (11.9)	1 (2.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.957 (0.580, 42.392)
	Treatment P-value [b]		0.10269
	Interaction P-value [c]		0.18780
Neuropathy	No. of Events (%)	23 (54.8)	16 (41.0)
	Median Survival Est. (95% CI)	4.63 (2.96, NC)	NC (3.94, NC)
	Hazard Ratio (95% CI) [a]		1.372 (0.725, 2.597)
	Treatment P-value [b]		0.32225
	Interaction P-value [c]		0.02171

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

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Table AESI.KM.S4.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Region, Level: US

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Ocular disorders	No. of Events (%)	13 (31.0)	9 (23.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.457 (0.623, 3.409)
	Treatment P-value [b]		0.36337
	Interaction P-value [c]		0.00371
Skin reactions	No. of Events (%)	27 (64.3)	12 (30.8)
	Median Survival Est. (95% CI)	1.23 (0.49, 4.99)	NC (8.97, NC)
	Hazard Ratio (95% CI) [a]		2.864 (1.450, 5.659)
	Treatment P-value [b]		0.00115
	Interaction P-value [c]		0.75820

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

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Table AESI.KM.S4.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Region, Level: Rest of the World

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Hyperglycemia	No. of Events (%)	11 (8.3)	3 (2.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.752 (1.047, 13.450)
	Treatment P-value [b]		0.03103
	Interaction P-value [c]		0.98231

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

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Table AESI.KM.S4.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Region, Level: Rest of the World

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Infusion related reaction	No. of Events (%)	17 (12.9)	9 (7.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.901 (0.847, 4.266)
	Treatment P-value [b]		0.11492
	Interaction P-value [c]		0.18780
Neuropathy	No. of Events (%)	65 (49.2)	54 (41.9)
	Median Survival Est. (95% CI)	6.34 (4.83, NC)	NC (3.68, NC)
	Hazard Ratio (95% CI) [a]		1.023 (0.713, 1.468)
	Treatment P-value [b]		0.88271
	Interaction P-value [c]		0.02171

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

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Table AESI.KM.S4.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Region, Level: Rest of the World

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Ocular disorders	No. of Events (%)	22 (16.7)	9 (7.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.489 (1.146, 5.407)
	Treatment P-value [b]		0.01726
	Interaction P-value [c]		0.00371
Skin reactions	No. of Events (%)	81 (61.4)	34 (26.4)
	Median Survival Est. (95% CI)	1.05 (0.56, 2.56)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.321 (2.223, 4.961)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.75820

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

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Table AESI.KM.S5.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Hyperglycemia	No. of Events (%)	12 (10.0)	3 (2.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.161 (1.174, 14.745)
	Treatment P-value [b]		0.01609
	Interaction P-value [c]		0.89688

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

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Table AESI.KM.S5.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Infusion related reaction	No. of Events (%)	18 (15.0)	7 (5.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.649 (1.106, 6.343)
	Treatment P-value [b]		0.02360
	Interaction P-value [c]		0.07706
Neuropathy	No. of Events (%)	67 (55.8)	47 (39.5)
	Median Survival Est. (95% CI)	5.06 (3.71, 10.58)	NC (9.07, NC)
	Hazard Ratio (95% CI) [a]		1.440 (0.991, 2.092)
	Treatment P-value [b]		0.05573
	Interaction P-value [c]		0.97775

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESI.KM.S5.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Ocular disorders	No. of Events (%)	34 (28.3)	8 (6.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.842 (2.241, 10.459)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.47506
Skin reactions	No. of Events (%)	78 (65.0)	31 (26.1)
	Median Survival Est. (95% CI)	0.87 (0.49, 3.35)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.683 (2.426, 5.591)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.60903

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
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Table AESI.KM.S5.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Hyperglycemia	No. of Events (%)	23 (13.1)	5 (2.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.623 (1.758, 12.162)
	Treatment P-value [b]		0.00065
	Interaction P-value [c]		0.89688

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESI.KM.S5.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Infusion related reaction	No. of Events (%)	9 (5.1)	10 (5.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.854 (0.347, 2.103)
	Treatment P-value [b]		0.75411
	Interaction P-value [c]		0.07706
Neuropathy	No. of Events (%)	82 (46.6)	53 (30.8)
	Median Survival Est. (95% CI)	6.93 (4.60, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.450 (1.027, 2.049)
	Treatment P-value [b]		0.03428
	Interaction P-value [c]		0.97775

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESI.KM.S5.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Ocular disorders	No. of Events (%)	49 (27.8)	15 (8.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.409 (1.911, 6.079)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.47506
Skin reactions	No. of Events (%)	85 (48.3)	31 (18.0)
	Median Survival Est. (95% CI)	6.60 (2.33, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.161 (2.095, 4.771)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.60903

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AESI.KM.S6.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Hyperglycemia	No. of Events (%)	10 (10.9)	1 (1.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.982 (1.278, 77.955)
	Treatment P-value [b]		0.00684
	Interaction P-value [c]		0.37752

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Table AESI.KM.S6.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Infusion related reaction	No. of Events (%)	6 (6.5)	2 (2.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.871 (0.579, 14.226)
	Treatment P-value [b]		0.18462
	Interaction P-value [c]		0.41198
Neuropathy	No. of Events (%)	40 (43.5)	30 (34.5)
	Median Survival Est. (95% CI)	5.13 (4.07, NC)	NC (5.26, NC)
	Hazard Ratio (95% CI) [a]		1.228 (0.765, 1.971)
	Treatment P-value [b]		0.37308
	Interaction P-value [c]		0.42978

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESI.KM.S6.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Ocular disorders	No. of Events (%)	24 (26.1)	7 (8.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.514 (1.514, 8.157)
	Treatment P-value [b]		0.00176
	Interaction P-value [c]		0.76705
Skin reactions	No. of Events (%)	51 (55.4)	16 (18.4)
	Median Survival Est. (95% CI)	2.73 (0.92, 7.06)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.803 (2.168, 6.673)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.57645

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESI.KM.S6.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Hyperglycemia	No. of Events (%)	25 (12.3)	7 (3.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.675 (1.589, 8.496)
	Treatment P-value [b]		0.00110
	Interaction P-value [c]		0.37752

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AESI.KM.S6.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Infusion related reaction	No. of Events (%)	21 (10.3)	15 (7.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.390 (0.717, 2.697)
	Treatment P-value [b]		0.32196
	Interaction P-value [c]		0.41198
Neuropathy	No. of Events (%)	109 (53.4)	70 (34.3)
	Median Survival Est. (95% CI)	5.78 (4.60, 8.34)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.539 (1.140, 2.079)
	Treatment P-value [b]		0.00413
	Interaction P-value [c]		0.42978

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESI.KM.S6.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Ocular disorders	No. of Events (%)	59 (28.9)	16 (7.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.092 (2.355, 7.110)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.76705
Skin reactions	No. of Events (%)	112 (54.9)	46 (22.5)
	Median Survival Est. (95% CI)	3.61 (1.41, 12.68)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.153 (2.235, 4.446)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.57645

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Analysis Plan: 15FEB2021 Confidential

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Table AESI.KM.S7.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Hyperglycemia	No. of Events (%)	14 (10.0)	2 (1.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.507 (1.252, 24.233)
	Treatment P-value [b]		0.01132
	Interaction P-value [c]		0.42946

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AESI.KM.S7.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Infusion related reaction	No. of Events (%)	14 (10.0)	5 (4.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.119 (0.763, 5.885)
	Treatment P-value [b]		0.14464
	Interaction P-value [c]		0.35097
Neuropathy	No. of Events (%)	73 (52.1)	58 (54.2)
	Median Survival Est. (95% CI)	5.06 (4.21, 7.62)	2.79 (1.48, NC)
	Hazard Ratio (95% CI) [a]		0.704 (0.499, 0.994)
	Treatment P-value [b]		0.05033
	Interaction P-value [c]		<.00001

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESI.KM.S7.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Ocular disorders	No. of Events (%)	31 (22.1)	7 (6.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.653 (1.608, 8.296)
	Treatment P-value [b]		0.00086
	Interaction P-value [c]		0.01497
Skin reactions	No. of Events (%)	77 (55.0)	24 (22.4)
	Median Survival Est. (95% CI)	2.73 (1.31, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.106 (1.963, 4.912)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.71541

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESI.KM.S7.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Hyperglycemia	No. of Events (%)	12 (14.1)	2 (1.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		8.128 (1.819, 36.316)
	Treatment P-value [b]		0.00111
	Interaction P-value [c]		0.42946

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Analysis Plan: 15FEB2021 Confidential

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Table AESI.KM.S7.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Infusion related reaction	No. of Events (%)	10 (11.8)	7 (6.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.885 (0.717, 4.952)
	Treatment P-value [b]		0.18296
	Interaction P-value [c]		0.35097
Neuropathy	No. of Events (%)	41 (48.2)	29 (26.6)
	Median Survival Est. (95% CI)	8.31 (4.21, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.864 (1.159, 2.999)
	Treatment P-value [b]		0.00855
	Interaction P-value [c]		<.00001

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Table AESI.KM.S7.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Ocular disorders	No. of Events (%)	22 (25.9)	14 (12.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.045 (1.046, 3.997)
	Treatment P-value [b]		0.03219
	Interaction P-value [c]		0.01497
Skin reactions	No. of Events (%)	54 (63.5)	29 (26.6)
	Median Survival Est. (95% CI)	0.99 (0.46, 4.50)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.397 (2.161, 5.339)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.71541

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Table AESI.KM.S7.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Hyperglycemia	No. of Events (%)	9 (12.7)	4 (5.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.440 (0.751, 7.925)
	Treatment P-value [b]		0.12105
	Interaction P-value [c]		0.42946

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
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Table AESI.KM.S7.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Infusion related reaction	No. of Events (%)	3 (4.2)	5 (6.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.619 (0.148, 2.589)
	Treatment P-value [b]		0.50599
	Interaction P-value [c]		0.35097
Neuropathy	No. of Events (%)	35 (49.3)	13 (17.3)
	Median Survival Est. (95% CI)	5.78 (2.89, 11.99)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.660 (1.935, 6.920)
	Treatment P-value [b]		0.00002
	Interaction P-value [c]		<.00001

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESI.KM.S7.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Ocular disorders	No. of Events (%)	30 (42.3)	2 (2.7)
	Median Survival Est. (95% CI)	9.95 (3.94, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		20.908 (4.995, 87.518)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.01497
Skin reactions	No. of Events (%)	32 (45.1)	9 (12.0)
	Median Survival Est. (95% CI)	12.68 (2.30, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.464 (2.130, 9.355)
	Treatment P-value [b]		0.00001
	Interaction P-value [c]		0.71541

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESI.KM.S8.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Hyperglycemia	No. of Events (%)	12 (12.5)	5 (4.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.633 (0.928, 7.475)
	Treatment P-value [b]		0.06190
	Interaction P-value [c]		0.19547

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESI.KM.S8.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Infusion related reaction	No. of Events (%)	8 (8.3)	4 (3.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.134 (0.643, 7.088)
	Treatment P-value [b]		0.20968
	Interaction P-value [c]		0.53564
Neuropathy	No. of Events (%)	52 (54.2)	37 (36.3)
	Median Survival Est. (95% CI)	5.13 (3.75, 8.31)	NC (5.26, NC)
	Hazard Ratio (95% CI) [a]		1.452 (0.952, 2.214)
	Treatment P-value [b]		0.07828
	Interaction P-value [c]		0.98165

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESI.KM.S8.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Ocular disorders	No. of Events (%)	23 (24.0)	7 (6.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.712 (1.593, 8.651)
	Treatment P-value [b]		0.00123
	Interaction P-value [c]		0.89134
Skin reactions	No. of Events (%)	61 (63.5)	23 (22.5)
	Median Survival Est. (95% CI)	1.35 (0.59, 3.78)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.791 (2.345, 6.130)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.52994

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESI.KM.S8.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Hyperglycemia	No. of Events (%)	23 (11.5)	3 (1.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.539 (2.264, 25.109)
	Treatment P-value [b]		0.00010
	Interaction P-value [c]		0.19547

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESI.KM.S8.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Infusion related reaction	No. of Events (%)	19 (9.5)	13 (6.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.375 (0.679, 2.784)
	Treatment P-value [b]		0.37510
	Interaction P-value [c]		0.53564
Neuropathy	No. of Events (%)	97 (48.5)	63 (33.3)
	Median Survival Est. (95% CI)	6.93 (4.40, 11.99)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.443 (1.051, 1.982)
	Treatment P-value [b]		0.02195
	Interaction P-value [c]		0.98165

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESI.KM.S8.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Ocular disorders	No. of Events (%)	60 (30.0)	16 (8.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.983 (2.294, 6.914)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.89134
Skin reactions	No. of Events (%)	102 (51.0)	39 (20.6)
	Median Survival Est. (95% CI)	5.98 (2.17, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.123 (2.158, 4.518)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.52994

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESI.KM.S9.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Hyperglycemia	No. of Events (%)	32 (12.4)	8 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.085 (1.882, 8.865)
	Treatment P-value [b]		0.00011
	Interaction P-value [c]		0.98604

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESI.KM.S9.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Infusion related reaction	No. of Events (%)	23 (8.9)	15 (5.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.502 (0.783, 2.879)
	Treatment P-value [b]		0.21310
	Interaction P-value [c]		0.75867
Neuropathy	No. of Events (%)	130 (50.2)	89 (34.9)
	Median Survival Est. (95% CI)	6.21 (4.63, 8.61)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.399 (1.068, 1.832)
	Treatment P-value [b]		0.01415
	Interaction P-value [c]		0.52335

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESI.KM.S9.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Ocular disorders	No. of Events (%)	76 (29.3)	20 (7.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.188 (2.559, 6.855)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.41108
Skin reactions	No. of Events (%)	143 (55.2)	49 (19.2)
	Median Survival Est. (95% CI)	3.35 (1.45, 7.49)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.743 (2.704, 5.181)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.05138

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESI.KM.S9.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Hyperglycemia	No. of Events (%)	3 (8.1)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.08167
	Interaction P-value [c]		0.98604

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESI.KM.S9.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Infusion related reaction	No. of Events (%)	4 (10.8)	2 (5.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.997 (0.366, 10.904)
	Treatment P-value [b]		0.43073
	Interaction P-value [c]		0.75867
Neuropathy	No. of Events (%)	19 (51.4)	11 (30.6)
	Median Survival Est. (95% CI)	4.83 (3.22, NC)	NC (4.44, NC)
	Hazard Ratio (95% CI) [a]		1.809 (0.861, 3.801)
	Treatment P-value [b]		0.13498
	Interaction P-value [c]		0.52335

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESI.KM.S9.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Ocular disorders	No. of Events (%)	7 (18.9)	3 (8.3)
	Median Survival Est. (95% CI)	NC (9.66, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.290 (0.592, 8.856)
	Treatment P-value [b]		0.21265
	Interaction P-value [c]		0.41108
Skin reactions	No. of Events (%)	20 (54.1)	13 (36.1)
	Median Survival Est. (95% CI)	2.79 (0.59, NC)	NC (2.10, NC)
	Hazard Ratio (95% CI) [a]		1.741 (0.866, 3.501)
	Treatment P-value [b]		0.14112
	Interaction P-value [c]		0.05138

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESI.KM.S10.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Hyperglycemia	No. of Events (%)	8 (13.1)	1 (2.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.769 (0.847, 54.120)
	Treatment P-value [b]		0.03712
	Interaction P-value [c]		0.52158

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESI.KM.S10.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Infusion related reaction	No. of Events (%)	9 (14.8)	4 (8.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.870 (0.576, 6.072)
	Treatment P-value [b]		0.27531
	Interaction P-value [c]		0.88598
Neuropathy	No. of Events (%)	34 (55.7)	17 (34.7)
	Median Survival Est. (95% CI)	4.60 (2.99, NC)	NC (5.49, NC)
	Hazard Ratio (95% CI) [a]		1.636 (0.914, 2.930)
	Treatment P-value [b]		0.10048
	Interaction P-value [c]		0.65398

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table AESI.KM.S10.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Ocular disorders	No. of Events (%)	15 (24.6)	2 (4.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.433 (1.471, 28.132)
	Treatment P-value [b]		0.00437
	Interaction P-value [c]		0.56459
Skin reactions	No. of Events (%)	38 (62.3)	11 (22.4)
	Median Survival Est. (95% CI)	1.31 (0.49, 4.04)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.074 (2.080, 7.977)
	Treatment P-value [b]		0.00001
	Interaction P-value [c]		0.57782

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table AESI.KM.S10.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Hyperglycemia	No. of Events (%)	22 (10.9)	7 (3.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.247 (1.387, 7.602)
	Treatment P-value [b]		0.00421
	Interaction P-value [c]		0.52158

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table AESI.KM.S10.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Infusion related reaction	No. of Events (%)	17 (8.4)	10 (5.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.686 (0.772, 3.683)
	Treatment P-value [b]		0.18737
	Interaction P-value [c]		0.88598
Neuropathy	No. of Events (%)	99 (49.0)	69 (34.2)
	Median Survival Est. (95% CI)	6.60 (4.63, 11.99)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.407 (1.035, 1.914)
	Treatment P-value [b]		0.02811
	Interaction P-value [c]		0.65398

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
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Astellas: 7465-CL-0301
Table AESI.KM.S10.SAF: Time to First AESI (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Ocular disorders	No. of Events (%)	61 (30.2)	17 (8.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.055 (2.368, 6.943)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.56459
Skin reactions	No. of Events (%)	112 (55.4)	44 (21.8)
	Median Survival Est. (95% CI)	2.56 (1.35, 7.49)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.286 (2.317, 4.661)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.57782

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Astellas: 7465-CL-0301
Table AESINSV.KM.S1.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Hyperglycemia	No. of Events (%)	5 (4.7)	1 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.795 (0.560, 41.043)
	Treatment P-value [b]		0.11638
	Interaction P-value [c]		0.79161

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
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Astellas: 7465-CL-0301
Table AESINSV.KM.S1.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Infusion related reaction	No. of Events (%)	7 (6.6)	6 (5.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.108 (0.372, 3.296)
	Treatment P-value [b]		0.83538
	Interaction P-value [c]		0.61903
Neuropathy	No. of Events (%)	52 (49.1)	36 (35.0)
	Median Survival Est. (95% CI)	6.93 (5.13, NC)	NC (9.07, NC)
	Hazard Ratio (95% CI) [a]		1.301 (0.850, 1.989)
	Treatment P-value [b]		0.20789
	Interaction P-value [c]		0.47834

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AESINSV.KM.S1.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Ocular disorders	No. of Events (%)	20 (18.9)	7 (6.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.839 (1.201, 6.715)
	Treatment P-value [b]		0.01232
	Interaction P-value [c]		0.41496
Skin reactions	No. of Events (%)	52 (49.1)	21 (20.4)
	Median Survival Est. (95% CI)	8.15 (1.54, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.987 (1.799, 4.960)
	Treatment P-value [b]		0.00001
	Interaction P-value [c]		0.76770

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AESINSV.KM.S1.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Hyperglycemia	No. of Events (%)	17 (8.9)	5 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.485 (1.286, 9.446)
	Treatment P-value [b]		0.00907
	Interaction P-value [c]		0.79161

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AESINSV.KM.S1.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Infusion related reaction	No. of Events (%)	17 (8.9)	11 (5.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.552 (0.727, 3.313)
	Treatment P-value [b]		0.25484
	Interaction P-value [c]		0.61903
Neuropathy	No. of Events (%)	97 (51.1)	63 (33.5)
	Median Survival Est. (95% CI)	4.86 (4.04, 7.92)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.576 (1.147, 2.165)
	Treatment P-value [b]		0.00528
	Interaction P-value [c]		0.47834

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Table AESINSV.KM.S1.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Ocular disorders	No. of Events (%)	61 (32.1)	16 (8.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.343 (2.504, 7.534)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.41496
Skin reactions	No. of Events (%)	104 (54.7)	40 (21.3)
	Median Survival Est. (95% CI)	2.79 (1.45, 11.86)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.282 (2.278, 4.730)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.76770

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Analysis Plan: 15FEB2021 Confidential

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Table AESINSV.KM.S2.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Hyperglycemia	No. of Events (%)	15 (6.1)	4 (1.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.444 (1.143, 10.377)
	Treatment P-value [b]		0.01935
	Interaction P-value [c]		0.70718

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

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Table AESINSV.KM.S2.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Infusion related reaction	No. of Events (%)	24 (9.8)	10 (4.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.226 (1.064, 4.655)
	Treatment P-value [b]		0.02890
	Interaction P-value [c]		0.98697
Neuropathy	No. of Events (%)	126 (51.4)	77 (34.1)
	Median Survival Est. (95% CI)	5.55 (4.60, 8.31)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.483 (1.117, 1.970)
	Treatment P-value [b]		0.00562
	Interaction P-value [c]		0.78624

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Table AESINSV.KM.S2.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Ocular disorders	No. of Events (%)	62 (25.3)	16 (7.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.831 (2.211, 6.638)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.81517
Skin reactions	No. of Events (%)	131 (53.5)	48 (21.2)
	Median Survival Est. (95% CI)	4.04 (1.68, 11.86)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.202 (2.300, 4.460)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.84496

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESINSV.KM.S2.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Hyperglycemia	No. of Events (%)	7 (13.7)	2 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.976 (1.034, 23.958)
	Treatment P-value [b]		0.02728
	Interaction P-value [c]		0.70718

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AESINSV.KM.S2.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Infusion related reaction	No. of Events (%)	0	7 (10.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.01927
	Interaction P-value [c]		0.98697
Neuropathy	No. of Events (%)	23 (45.1)	22 (33.8)
	Median Survival Est. (95% CI)	7.92 (3.68, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.356 (0.756, 2.433)
	Treatment P-value [b]		0.32018
	Interaction P-value [c]		0.78624

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table AESINSV.KM.S2.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Ocular disorders	No. of Events (%)	19 (37.3)	7 (10.8)
	Median Survival Est. (95% CI)	NC (3.94, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.330 (1.819, 10.306)
	Treatment P-value [b]		0.00040
	Interaction P-value [c]		0.81517
Skin reactions	No. of Events (%)	25 (49.0)	13 (20.0)
	Median Survival Est. (95% CI)	3.68 (1.25, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.972 (1.520, 5.813)
	Treatment P-value [b]		0.00081
	Interaction P-value [c]		0.84496

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
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Astellas: 7465-CL-0301
Table AESINSV.KM.S3.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Hyperglycemia	No. of Events (%)	20 (8.5)	4 (1.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.741 (1.620, 13.870)
	Treatment P-value [b]		0.00170
	Interaction P-value [c]		0.22665

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESINSV.KM.S3.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Infusion related reaction	No. of Events (%)	17 (7.3)	13 (5.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.207 (0.586, 2.486)
	Treatment P-value [b]		0.61912
	Interaction P-value [c]		0.43271
Neuropathy	No. of Events (%)	123 (52.6)	71 (32.4)
	Median Survival Est. (95% CI)	5.29 (4.21, 8.31)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.652 (1.233, 2.212)
	Treatment P-value [b]		0.00062
	Interaction P-value [c]		0.09338

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

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Table AESINSV.KM.S3.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Ocular disorders	No. of Events (%)	67 (28.6)	17 (7.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.019 (2.360, 6.844)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.62942
Skin reactions	No. of Events (%)	124 (53.0)	42 (19.2)
	Median Survival Est. (95% CI)	4.04 (1.68, 12.68)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.534 (2.490, 5.018)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.23873

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

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Table AESINSV.KM.S3.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Any	No. of Events (%)	41 (66.1)	42 (58.3)
	Median Survival Est. (95% CI)	1.41 (0.66, 2.37)	2.73 (0.79, 6.51)
	Hazard Ratio (95% CI) [a]		1.254 (0.815, 1.928)
	Treatment P-value [b]		0.36626
	Interaction P-value [c]		0.02060
Hyperglycemia	No. of Events (%)	2 (3.2)	2 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.194 (0.168, 8.479)
	Treatment P-value [b]		0.84587
	Interaction P-value [c]		0.22665

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESINSV.KM.S3.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Infusion related reaction	No. of Events (%)	7 (11.3)	4 (5.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.135 (0.625, 7.295)
	Treatment P-value [b]		0.21873
	Interaction P-value [c]		0.43271
Neuropathy	No. of Events (%)	26 (41.9)	28 (38.9)
	Median Survival Est. (95% CI)	NC (4.63, NC)	NC (5.26, NC)
	Hazard Ratio (95% CI) [a]		0.981 (0.575, 1.673)
	Treatment P-value [b]		0.97073
	Interaction P-value [c]		0.09338

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

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Table AESINSV.KM.S3.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Ocular disorders	No. of Events (%)	14 (22.6)	6 (8.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.069 (1.179, 7.988)
	Treatment P-value [b]		0.01470
	Interaction P-value [c]		0.62942
Skin reactions	No. of Events (%)	32 (51.6)	19 (26.4)
	Median Survival Est. (95% CI)	6.60 (1.31, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.367 (1.341, 4.177)
	Treatment P-value [b]		0.00223
	Interaction P-value [c]		0.23873

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

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Table AESINSV.KM.S4.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Region, Level: Western Europe

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Hyperglycemia	No. of Events (%)	11 (9.0)	4 (3.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.736 (0.871, 8.594)
	Treatment P-value [b]		0.07165
	Interaction P-value [c]		0.99619

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESINSV.KM.S4.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Region, Level: Western Europe

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Infusion related reaction	No. of Events (%)	5 (4.1)	7 (5.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.686 (0.218, 2.160)
	Treatment P-value [b]		0.52819
	Interaction P-value [c]		0.23782
Neuropathy	No. of Events (%)	61 (50.0)	30 (24.4)
	Median Survival Est. (95% CI)	6.21 (3.29, 11.99)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.284 (1.474, 3.537)
	Treatment P-value [b]		0.00017
	Interaction P-value [c]		0.02968

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Analysis Plan: 15FEB2021 Confidential

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Table AESINSV.KM.S4.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Region, Level: Western Europe

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Ocular disorders	No. of Events (%)	48 (39.3)	5 (4.1)
	Median Survival Est. (95% CI)	NC (6.77, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		11.611 (4.620, 29.179)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.00185
Skin reactions	No. of Events (%)	52 (42.6)	16 (13.0)
	Median Survival Est. (95% CI)	12.68 (4.21, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.719 (2.124, 6.514)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.59083

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

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Table AESINSV.KM.S4.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Region, Level: US

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Hyperglycemia	No. of Events (%)	6 (14.3)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.01421
	Interaction P-value [c]		0.99619

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESINSV.KM.S4.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Region, Level: US

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Infusion related reaction	No. of Events (%)	5 (11.9)	1 (2.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.981 (0.582, 42.599)
	Treatment P-value [b]		0.10269
	Interaction P-value [c]		0.23782
Neuropathy	No. of Events (%)	23 (54.8)	16 (41.0)
	Median Survival Est. (95% CI)	4.63 (2.96, NC)	NC (3.94, NC)
	Hazard Ratio (95% CI) [a]		1.374 (0.726, 2.601)
	Treatment P-value [b]		0.32225
	Interaction P-value [c]		0.02968

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Table AESINSV.KM.S4.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Region, Level: US

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Ocular disorders	No. of Events (%)	11 (26.2)	9 (23.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.208 (0.501, 2.915)
	Treatment P-value [b]		0.64397
	Interaction P-value [c]		0.00185
Skin reactions	No. of Events (%)	24 (57.1)	12 (30.8)
	Median Survival Est. (95% CI)	3.68 (0.59, NC)	NC (8.97, NC)
	Hazard Ratio (95% CI) [a]		2.363 (1.181, 4.728)
	Treatment P-value [b]		0.00939
	Interaction P-value [c]		0.59083

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESINSV.KM.S4.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Region, Level: Rest of the World

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Hyperglycemia	No. of Events (%)	5 (3.8)	2 (1.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.506 (0.486, 12.917)
	Treatment P-value [b]		0.26562
	Interaction P-value [c]		0.99619

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table AESINSV.KM.S4.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Region, Level: Rest of the World

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Infusion related reaction	No. of Events (%)	14 (10.6)	9 (7.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.559 (0.675, 3.603)
	Treatment P-value [b]		0.29674
	Interaction P-value [c]		0.23782
Neuropathy	No. of Events (%)	65 (49.2)	53 (41.1)
	Median Survival Est. (95% CI)	6.34 (4.83, NC)	NC (3.94, NC)
	Hazard Ratio (95% CI) [a]		1.059 (0.737, 1.523)
	Treatment P-value [b]		0.74360
	Interaction P-value [c]		0.02968

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Astellas: 7465-CL-0301
Table AESINSV.KM.S4.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Region, Level: Rest of the World

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Ocular disorders	No. of Events (%)	22 (16.7)	9 (7.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.488 (1.146, 5.405)
	Treatment P-value [b]		0.01726
	Interaction P-value [c]		0.00185
Skin reactions	No. of Events (%)	80 (60.6)	33 (25.6)
	Median Survival Est. (95% CI)	1.35 (0.62, 3.06)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.345 (2.228, 5.023)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.59083

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESINSV.KM.S5.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Hyperglycemia	No. of Events (%)	8 (6.7)	3 (2.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.724 (0.723, 10.268)
	Treatment P-value [b]		0.12239
	Interaction P-value [c]		0.57310

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Table AESINSV.KM.S5.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Infusion related reaction	No. of Events (%)	15 (12.5)	7 (5.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.187 (0.892, 5.364)
	Treatment P-value [b]		0.08198
	Interaction P-value [c]		0.15181
Neuropathy	No. of Events (%)	67 (55.8)	46 (38.7)
	Median Survival Est. (95% CI)	5.13 (3.71, 10.58)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.491 (1.024, 2.170)
	Treatment P-value [b]		0.03739
	Interaction P-value [c]		0.92748

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Table AESINSV.KM.S5.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Ocular disorders	No. of Events (%)	32 (26.7)	8 (6.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.527 (2.086, 9.824)
	Treatment P-value [b]		0.00003
	Interaction P-value [c]		0.56593
Skin reactions	No. of Events (%)	75 (62.5)	30 (25.2)
	Median Survival Est. (95% CI)	1.41 (0.53, 5.98)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.560 (2.329, 5.442)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.54917

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Analysis Plan: 15FEB2021 Confidential

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Table AESINSV.KM.S5.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Hyperglycemia	No. of Events (%)	14 (8.0)	3 (1.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.598 (1.321, 16.000)
	Treatment P-value [b]		0.00826
	Interaction P-value [c]		0.57310

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AESINSV.KM.S5.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Infusion related reaction	No. of Events (%)	9 (5.1)	10 (5.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.863 (0.351, 2.125)
	Treatment P-value [b]		0.75411
	Interaction P-value [c]		0.15181
Neuropathy	No. of Events (%)	82 (46.6)	53 (30.8)
	Median Survival Est. (95% CI)	6.93 (4.60, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.456 (1.030, 2.056)
	Treatment P-value [b]		0.03239
	Interaction P-value [c]		0.92748

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Table AESINSV.KM.S5.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Ocular disorders	No. of Events (%)	49 (27.8)	15 (8.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.410 (1.912, 6.082)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.56593
Skin reactions	No. of Events (%)	81 (46.0)	31 (18.0)
	Median Survival Est. (95% CI)	NC (2.56, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.970 (1.963, 4.495)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.54917

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Table AESINSV.KM.S6.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Hyperglycemia	No. of Events (%)	6 (6.5)	1 (1.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.853 (0.705, 48.617)
	Treatment P-value [b]		0.06457
	Interaction P-value [c]		0.62004

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AESINSV.KM.S6.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Infusion related reaction	No. of Events (%)	5 (5.4)	2 (2.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.415 (0.469, 12.453)
	Treatment P-value [b]		0.26800
	Interaction P-value [c]		0.47019
Neuropathy	No. of Events (%)	40 (43.5)	30 (34.5)
	Median Survival Est. (95% CI)	5.29 (4.07, NC)	NC (5.26, NC)
	Hazard Ratio (95% CI) [a]		1.227 (0.764, 1.970)
	Treatment P-value [b]		0.37507
	Interaction P-value [c]		0.37974

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
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Table AESINSV.KM.S6.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Ocular disorders	No. of Events (%)	23 (25.0)	7 (8.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.346 (1.435, 7.801)
	Treatment P-value [b]		0.00292
	Interaction P-value [c]		0.72333
Skin reactions	No. of Events (%)	50 (54.3)	16 (18.4)
	Median Survival Est. (95% CI)	2.73 (0.95, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.690 (2.100, 6.482)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.53142

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESINSV.KM.S6.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Hyperglycemia	No. of Events (%)	16 (7.8)	5 (2.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.236 (1.185, 8.832)
	Treatment P-value [b]		0.01523
	Interaction P-value [c]		0.62004

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESINSV.KM.S6.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Infusion related reaction	No. of Events (%)	19 (9.3)	15 (7.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.256 (0.638, 2.472)
	Treatment P-value [b]		0.50342
	Interaction P-value [c]		0.47019
Neuropathy	No. of Events (%)	109 (53.4)	69 (33.8)
	Median Survival Est. (95% CI)	5.78 (4.60, 8.34)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.579 (1.167, 2.135)
	Treatment P-value [b]		0.00250
	Interaction P-value [c]		0.37974

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESINSV.KM.S6.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Ocular disorders	No. of Events (%)	58 (28.4)	16 (7.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.017 (2.309, 6.987)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.72333
Skin reactions	No. of Events (%)	106 (52.0)	45 (22.1)
	Median Survival Est. (95% CI)	5.98 (1.68, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.986 (2.106, 4.234)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.53142

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table AESINSV.KM.S7.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Hyperglycemia	No. of Events (%)	6 (4.3)	2 (1.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.283 (0.461, 11.313)
	Treatment P-value [b]		0.30076
	Interaction P-value [c]		0.31273

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table AESINSV.KM.S7.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Infusion related reaction	No. of Events (%)	11 (7.9)	5 (4.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.665 (0.578, 4.792)
	Treatment P-value [b]		0.34161
	Interaction P-value [c]		0.42955
Neuropathy	No. of Events (%)	73 (52.1)	57 (53.3)
	Median Survival Est. (95% CI)	5.29 (4.21, 7.62)	3.68 (1.54, NC)
	Hazard Ratio (95% CI) [a]		0.735 (0.520, 1.039)
	Treatment P-value [b]		0.08517
	Interaction P-value [c]		0.00001

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESINSV.KM.S7.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Ocular disorders	No. of Events (%)	31 (22.1)	7 (6.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.651 (1.608, 8.293)
	Treatment P-value [b]		0.00086
	Interaction P-value [c]		0.00996
Skin reactions	No. of Events (%)	74 (52.9)	23 (21.5)
	Median Survival Est. (95% CI)	4.11 (1.45, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.064 (1.918, 4.893)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.63834

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Table AESINSV.KM.S7.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Hyperglycemia	No. of Events (%)	10 (11.8)	1 (0.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		13.353 (1.709, 104.313)
	Treatment P-value [b]		0.00134
	Interaction P-value [c]		0.31273

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AESINSV.KM.S7.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Infusion related reaction	No. of Events (%)	10 (11.8)	7 (6.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.889 (0.719, 4.964)
	Treatment P-value [b]		0.18296
	Interaction P-value [c]		0.42955
Neuropathy	No. of Events (%)	41 (48.2)	29 (26.6)
	Median Survival Est. (95% CI)	8.31 (4.21, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.866 (1.160, 3.002)
	Treatment P-value [b]		0.00855
	Interaction P-value [c]		0.00001

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AESINSV.KM.S7.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Ocular disorders	No. of Events (%)	20 (23.5)	14 (12.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.842 (0.930, 3.647)
	Treatment P-value [b]		0.07409
	Interaction P-value [c]		0.00996
Skin reactions	No. of Events (%)	50 (58.8)	29 (26.6)
	Median Survival Est. (95% CI)	1.51 (0.56, 7.95)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.012 (1.905, 4.762)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.63834

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Table AESINSV.KM.S7.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Hyperglycemia	No. of Events (%)	6 (8.5)	3 (4.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.174 (0.544, 8.694)
	Treatment P-value [b]		0.25401
	Interaction P-value [c]		0.31273

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Infusion related reaction	No. of Events (%)	3 (4.2)	5 (6.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.623 (0.149, 2.608)
	Treatment P-value [b]		0.50599
	Interaction P-value [c]		0.42955
Neuropathy	No. of Events (%)	35 (49.3)	13 (17.3)
	Median Survival Est. (95% CI)	5.78 (2.89, 11.99)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.664 (1.938, 6.929)
	Treatment P-value [b]		0.00002
	Interaction P-value [c]		0.00001

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Ocular disorders	No. of Events (%)	30 (42.3)	2 (2.7)
	Median Survival Est. (95% CI)	9.95 (3.94, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		20.943 (5.003, 87.668)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.00996
Skin reactions	No. of Events (%)	32 (45.1)	9 (12.0)
	Median Survival Est. (95% CI)	12.68 (2.30, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.487 (2.141, 9.403)
	Treatment P-value [b]		0.00001
	Interaction P-value [c]		0.63834

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESINSV.KM.S8.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Hyperglycemia	No. of Events (%)	9 (9.4)	4 (3.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.444 (0.752, 7.935)
	Treatment P-value [b]		0.12919
	Interaction P-value [c]		0.33282

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESINSV.KM.S8.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Infusion related reaction	No. of Events (%)	6 (6.3)	4 (3.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.594 (0.450, 5.647)
	Treatment P-value [b]		0.45952
	Interaction P-value [c]		0.79084
Neuropathy	No. of Events (%)	52 (54.2)	36 (35.3)
	Median Survival Est. (95% CI)	5.13 (3.75, 8.31)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.516 (0.991, 2.320)
	Treatment P-value [b]		0.05195
	Interaction P-value [c]		0.86486

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Table AESINSV.KM.S8.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Ocular disorders	No. of Events (%)	22 (22.9)	7 (6.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.539 (1.512, 8.284)
	Treatment P-value [b]		0.00202
	Interaction P-value [c]		0.84829
Skin reactions	No. of Events (%)	58 (60.4)	22 (21.6)
	Median Survival Est. (95% CI)	1.68 (0.92, 6.60)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.621 (2.215, 5.920)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.52969

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESINSV.KM.S8.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Hyperglycemia	No. of Events (%)	13 (6.5)	2 (1.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.243 (1.409, 27.665)
	Treatment P-value [b]		0.00554
	Interaction P-value [c]		0.33282

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESINSV.KM.S8.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Infusion related reaction	No. of Events (%)	18 (9.0)	13 (6.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.309 (0.641, 2.672)
	Treatment P-value [b]		0.46426
	Interaction P-value [c]		0.79084
Neuropathy	No. of Events (%)	97 (48.5)	63 (33.3)
	Median Survival Est. (95% CI)	6.93 (4.40, 11.99)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.448 (1.054, 1.989)
	Treatment P-value [b]		0.02058
	Interaction P-value [c]		0.86486

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
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Table AESINSV.KM.S8.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Ocular disorders	No. of Events (%)	59 (29.5)	16 (8.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.907 (2.248, 6.789)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.84829
Skin reactions	No. of Events (%)	98 (49.0)	39 (20.6)
	Median Survival Est. (95% CI)	7.49 (2.33, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.973 (2.050, 4.310)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.52969

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table AESINSV.KM.S9.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Hyperglycemia	No. of Events (%)	20 (7.7)	6 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.340 (1.341, 8.318)
	Treatment P-value [b]		0.00598
	Interaction P-value [c]		0.98843

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table AESINSV.KM.S9.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Infusion related reaction	No. of Events (%)	21 (8.1)	15 (5.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.374 (0.708, 2.665)
	Treatment P-value [b]		0.34419
	Interaction P-value [c]		0.92546
Neuropathy	No. of Events (%)	130 (50.2)	88 (34.5)
	Median Survival Est. (95% CI)	6.21 (4.63, 8.61)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.427 (1.088, 1.870)
	Treatment P-value [b]		0.00955
	Interaction P-value [c]		0.55378

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table AESINSV.KM.S9.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Ocular disorders	No. of Events (%)	74 (28.6)	20 (7.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.065 (2.480, 6.663)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.43516
Skin reactions	No. of Events (%)	137 (52.9)	49 (19.2)
	Median Survival Est. (95% CI)	4.04 (1.91, 12.68)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.507 (2.529, 4.863)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.10493

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AESINSV.KM.S9.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Hyperglycemia	No. of Events (%)	2 (5.4)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.16014
	Interaction P-value [c]		0.98843

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

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Table AESINSV.KM.S9.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Infusion related reaction	No. of Events (%)	3 (8.1)	2 (5.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.505 (0.251, 9.004)
	Treatment P-value [b]		0.64963
	Interaction P-value [c]		0.92546
Neuropathy	No. of Events (%)	19 (51.4)	11 (30.6)
	Median Survival Est. (95% CI)	4.83 (3.22, NC)	NC (4.44, NC)
	Hazard Ratio (95% CI) [a]		1.812 (0.862, 3.807)
	Treatment P-value [b]		0.13498
	Interaction P-value [c]		0.55378

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AESINSV.KM.S9.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Ocular disorders	No. of Events (%)	7 (18.9)	3 (8.3)
	Median Survival Est. (95% CI)	NC (9.66, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.291 (0.592, 8.860)
	Treatment P-value [b]		0.21265
	Interaction P-value [c]		0.43516
Skin reactions	No. of Events (%)	19 (51.4)	12 (33.3)
	Median Survival Est. (95% CI)	5.98 (0.59, NC)	NC (3.71, NC)
	Hazard Ratio (95% CI) [a]		1.820 (0.883, 3.750)
	Treatment P-value [b]		0.12445
	Interaction P-value [c]		0.10493

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

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Table AESINSV.KM.S10.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Hyperglycemia	No. of Events (%)	5 (8.2)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.04306
	Interaction P-value [c]		0.99051

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AESINSV.KM.S10.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Infusion related reaction	No. of Events (%)	8 (13.1)	4 (8.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.645 (0.495, 5.464)
	Treatment P-value [b]		0.38926
	Interaction P-value [c]		0.89627
Neuropathy	No. of Events (%)	34 (55.7)	17 (34.7)
	Median Survival Est. (95% CI)	4.60 (2.99, NC)	NC (5.49, NC)
	Hazard Ratio (95% CI) [a]		1.636 (0.914, 2.930)
	Treatment P-value [b]		0.10048
	Interaction P-value [c]		0.71137

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

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Table AESINSV.KM.S10.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Ocular disorders	No. of Events (%)	15 (24.6)	2 (4.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.435 (1.472, 28.139)
	Treatment P-value [b]		0.00437
	Interaction P-value [c]		0.53335
Skin reactions	No. of Events (%)	37 (60.7)	11 (22.4)
	Median Survival Est. (95% CI)	1.41 (0.59, 11.86)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.828 (1.951, 7.509)
	Treatment P-value [b]		0.00003
	Interaction P-value [c]		0.63213

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AESINSV.KM.S10.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Hyperglycemia	No. of Events (%)	14 (6.9)	6 (3.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.367 (0.909, 6.159)
	Treatment P-value [b]		0.06898
	Interaction P-value [c]		0.99051

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

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Table AESINSV.KM.S10.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Infusion related reaction	No. of Events (%)	15 (7.4)	10 (5.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.495 (0.671, 3.327)
	Treatment P-value [b]		0.32493
	Interaction P-value [c]		0.89627
Neuropathy	No. of Events (%)	99 (49.0)	68 (33.7)
	Median Survival Est. (95% CI)	6.60 (4.63, 11.99)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.445 (1.061, 1.967)
	Treatment P-value [b]		0.01854
	Interaction P-value [c]		0.71137

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

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Table AESINSV.KM.S10.SAF: Time to First Not Severe AESI (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Ocular disorders	No. of Events (%)	59 (29.2)	17 (8.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.906 (2.277, 6.700)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.53335
Skin reactions	No. of Events (%)	107 (53.0)	43 (21.3)
	Median Survival Est. (95% CI)	3.68 (1.54, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.179 (2.230, 4.532)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.63213

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

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Astellas: 7465-CL-0301
Table AESISV.KM.S1.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Hyperglycemia	No. of Events (%)	3 (2.8)	1 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.867 (0.298, 27.566)
	Treatment P-value [b]		0.34012
	Interaction P-value [c]		0.39335

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AESISV.KM.S1.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Neuropathy	No. of Events (%)	8 (7.5)	1 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.921 (0.866, 55.344)
	Treatment P-value [b]		0.03483
	Interaction P-value [c]		0.08292
Skin reactions	No. of Events (%)	13 (12.3)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00031
	Interaction P-value [c]		0.98678

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
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Astellas: 7465-CL-0301
Table AESISV.KM.S1.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Hyperglycemia	No. of Events (%)	18 (9.5)	2 (1.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.268 (2.150, 39.944)
	Treatment P-value [b]		0.00028
	Interaction P-value [c]		0.39335

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESISV.KM.S1.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Neuropathy	No. of Events (%)	8 (4.2)	8 (4.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.906 (0.340, 2.415)
	Treatment P-value [b]		0.88976
	Interaction P-value [c]		0.08292
Skin reactions	No. of Events (%)	32 (16.8)	2 (1.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		17.010 (4.076, 70.985)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.98678

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESISV.KM.S2.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Hyperglycemia	No. of Events (%)	15 (6.1)	2 (0.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.991 (1.599, 30.572)
	Treatment P-value [b]		0.00263
	Interaction P-value [c]		0.91383

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

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Table AESISV.KM.S2.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Neuropathy	No. of Events (%)	11 (4.5)	5 (2.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.804 (0.627, 5.194)
	Treatment P-value [b]		0.27726
	Interaction P-value [c]		0.86067
Skin reactions	No. of Events (%)	37 (15.1)	2 (0.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		17.745 (4.277, 73.628)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.98885

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

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Table AESISV.KM.S2.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Hyperglycemia	No. of Events (%)	6 (11.8)	1 (1.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		8.062 (0.970, 66.971)
	Treatment P-value [b]		0.02332
	Interaction P-value [c]		0.91383

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

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Table AESISV.KM.S2.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Neuropathy	No. of Events (%)	5 (9.8)	4 (6.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.551 (0.416, 5.782)
	Treatment P-value [b]		0.45421
	Interaction P-value [c]		0.86067
Skin reactions	No. of Events (%)	8 (15.7)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00089
	Interaction P-value [c]		0.98885

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESISV.KM.S3.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Hyperglycemia	No. of Events (%)	19 (8.1)	3 (1.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.018 (1.781, 20.338)
	Treatment P-value [b]		0.00099
	Interaction P-value [c]		0.99146

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

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Table AESISV.KM.S3.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Neuropathy	No. of Events (%)	16 (6.8)	7 (3.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.860 (0.765, 4.525)
	Treatment P-value [b]		0.16920
	Interaction P-value [c]		0.98980
Skin reactions	No. of Events (%)	38 (16.2)	1 (0.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		37.650 (5.170, 274.196)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.31225

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESISV.KM.S3.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Hyperglycemia	No. of Events (%)	2 (3.2)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.12596
	Interaction P-value [c]		0.99146

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

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Table AESISV.KM.S3.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Neuropathy	No. of Events (%)	0	2 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.19294
	Interaction P-value [c]		0.98980
Skin reactions	No. of Events (%)	7 (11.3)	1 (1.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		8.500 (1.046, 69.092)
	Treatment P-value [b]		0.01671
	Interaction P-value [c]		0.31225

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESISV.KM.S4.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Region, Level: Western Europe

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Hyperglycemia	No. of Events (%)	10 (8.2)	1 (0.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.986 (1.278, 78.010)
	Treatment P-value [b]		0.00655
	Interaction P-value [c]		0.66439

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

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Table AESISV.KM.S4.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Region, Level: Western Europe

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Neuropathy	No. of Events (%)	12 (9.8)	2 (1.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.697 (1.275, 25.455)
	Treatment P-value [b]		0.00981
	Interaction P-value [c]		0.01695
Skin reactions	No. of Events (%)	14 (11.5)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00016
	Interaction P-value [c]		0.99986

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

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Table AESISV.KM.S4.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Region, Level: US

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Hyperglycemia	No. of Events (%)	5 (11.9)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.02718
	Interaction P-value [c]		0.66439

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Analysis Plan: 15FEB2021 Confidential

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Table AESISV.KM.S4.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Region, Level: US

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Neuropathy	No. of Events (%)	2 (4.8)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.19972
	Interaction P-value [c]		0.01695
Skin reactions	No. of Events (%)	12 (28.6)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00035
	Interaction P-value [c]		0.99986

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

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Table AESISV.KM.S4.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Region, Level: Rest of the World

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Hyperglycemia	No. of Events (%)	6 (4.5)	2 (1.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.002 (0.606, 14.875)
	Treatment P-value [b]		0.15627
	Interaction P-value [c]		0.66439

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Analysis Plan: 15FEB2021 Confidential

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Table AESISV.KM.S4.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Region, Level: Rest of the World

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Neuropathy	No. of Events (%)	2 (1.5)	7 (5.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.241 (0.050, 1.161)
	Treatment P-value [b]		0.05499
	Interaction P-value [c]		0.01695
Skin reactions	No. of Events (%)	19 (14.4)	2 (1.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.966 (2.321, 42.790)
	Treatment P-value [b]		0.00015
	Interaction P-value [c]		0.99986

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESISV.KM.S5.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Hyperglycemia	No. of Events (%)	8 (6.7)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00420
	Interaction P-value [c]		0.98776

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESISV.KM.S5.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 0

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Neuropathy	No. of Events (%)	5 (4.2)	6 (5.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.802 (0.245, 2.630)
	Treatment P-value [b]		0.72805
	Interaction P-value [c]		0.13265
Skin reactions	No. of Events (%)	24 (20.0)	2 (1.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		13.254 (3.132, 56.090)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.98372

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESISV.KM.S5.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Hyperglycemia	No. of Events (%)	13 (7.4)	3 (1.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.268 (1.216, 14.979)
	Treatment P-value [b]		0.01380
	Interaction P-value [c]		0.98776

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESISV.KM.S5.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: ECOG PS from IRT Strata, Level: 1

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Neuropathy	No. of Events (%)	11 (6.3)	3 (1.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.057 (0.852, 10.963)
	Treatment P-value [b]		0.07142
	Interaction P-value [c]		0.13265
Skin reactions	No. of Events (%)	21 (11.9)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.98372

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESISV.KM.S6.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Hyperglycemia	No. of Events (%)	6 (6.5)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.01521
	Interaction P-value [c]		0.98979

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESISV.KM.S6.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: Yes

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Neuropathy	No. of Events (%)	3 (3.3)	4 (4.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.548 (0.122, 2.457)
	Treatment P-value [b]		0.50855
	Interaction P-value [c]		0.10438
Skin reactions	No. of Events (%)	14 (15.2)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00017
	Interaction P-value [c]		0.98751

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESISV.KM.S6.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Hyperglycemia	No. of Events (%)	15 (7.4)	3 (1.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.049 (1.462, 17.440)
	Treatment P-value [b]		0.00437
	Interaction P-value [c]		0.98979

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESISV.KM.S6.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Liver Metastasis from IRT Strata, Level: No

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Neuropathy	No. of Events (%)	13 (6.4)	5 (2.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.477 (0.883, 6.948)
	Treatment P-value [b]		0.07436
	Interaction P-value [c]		0.10438
Skin reactions	No. of Events (%)	31 (15.2)	2 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		16.333 (3.909, 68.248)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.98751

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

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Table AESISV.KM.S7.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Hyperglycemia	No. of Events (%)	10 (7.1)	1 (0.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.745 (0.991, 60.504)
	Treatment P-value [b]		0.02104
	Interaction P-value [c]		0.99110

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

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Table AESISV.KM.S7.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Paclitaxel

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Neuropathy	No. of Events (%)	9 (6.4)	9 (8.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.655 (0.260, 1.650)
	Treatment P-value [b]		0.36239
	Interaction P-value [c]		0.99993
Skin reactions	No. of Events (%)	24 (17.1)	1 (0.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		19.342 (2.617, 142.985)
	Treatment P-value [b]		0.00004
	Interaction P-value [c]		0.99991

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESISV.KM.S7.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Any	No. of Events (%)	18 (21.2)	3 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		8.514 (2.508, 28.907)
	Treatment P-value [b]		0.00004
	Interaction P-value [c]		0.08108
Hyperglycemia	No. of Events (%)	5 (5.9)	1 (0.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.587 (0.770, 56.381)
	Treatment P-value [b]		0.04640
	Interaction P-value [c]		0.99110

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

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Table AESISV.KM.S7.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Docetaxel

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Neuropathy	No. of Events (%)	1 (1.2)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.27699
	Interaction P-value [c]		0.99993
Skin reactions	No. of Events (%)	14 (16.5)	1 (0.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		19.403 (2.551, 147.555)
	Treatment P-value [b]		0.00007
	Interaction P-value [c]		0.99991

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

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Table AESISV.KM.S7.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Hyperglycemia	No. of Events (%)	6 (8.5)	1 (1.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.446 (0.776, 53.543)
	Treatment P-value [b]		0.04603
	Interaction P-value [c]		0.99110

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
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[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

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Table AESISV.KM.S7.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Pre-selected Investigator's Choice of Paclitaxel/Docetaxel/Vinflunine, Level: Vinflunine

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Neuropathy	No. of Events (%)	6 (8.5)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.01143
	Interaction P-value [c]		0.99993
Skin reactions	No. of Events (%)	7 (9.9)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00527
	Interaction P-value [c]		0.99991

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table AESISV.KM.S8.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Hyperglycemia	No. of Events (%)	6 (6.3)	2 (2.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.190 (0.644, 15.807)
	Treatment P-value [b]		0.13593
	Interaction P-value [c]		0.24838

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
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Astellas: 7465-CL-0301
Table AESISV.KM.S8.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Neuropathy	No. of Events (%)	3 (3.1)	4 (3.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.734 (0.164, 3.280)
	Treatment P-value [b]		0.68447
	Interaction P-value [c]		0.23572
Skin reactions	No. of Events (%)	17 (17.7)	1 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		19.381 (2.579, 145.650)
	Treatment P-value [b]		0.00006
	Interaction P-value [c]		0.80367

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table AESISV.KM.S8.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Hyperglycemia	No. of Events (%)	15 (7.5)	1 (0.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		14.577 (1.927, 110.286)
	Treatment P-value [b]		0.00057
	Interaction P-value [c]		0.24838

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table AESISV.KM.S8.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Neuropathy	No. of Events (%)	13 (6.5)	5 (2.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.205 (0.786, 6.187)
	Treatment P-value [b]		0.12606
	Interaction P-value [c]		0.23572
Skin reactions	No. of Events (%)	28 (14.0)	1 (0.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		27.774 (3.779, 204.128)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.80367

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table AESISV.KM.S9.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Hyperglycemia	No. of Events (%)	20 (7.7)	3 (1.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.687 (1.987, 22.504)
	Treatment P-value [b]		0.00038
	Interaction P-value [c]		0.99086

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table AESISV.KM.S9.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Neuropathy	No. of Events (%)	15 (5.8)	8 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.678 (0.711, 3.958)
	Treatment P-value [b]		0.23255
	Interaction P-value [c]		0.65698
Skin reactions	No. of Events (%)	41 (15.8)	1 (0.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		42.998 (5.917, 312.470)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.11082

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
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Table AESISV.KM.S9.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Hyperglycemia	No. of Events (%)	1 (2.7)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.31731
	Interaction P-value [c]		0.99086

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table AESISV.KM.S9.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Neuropathy	No. of Events (%)	1 (2.7)	1 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.869 (0.054, 13.901)
	Treatment P-value [b]		0.91762
	Interaction P-value [c]		0.65698
Skin reactions	No. of Events (%)	4 (10.8)	1 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.883 (0.434, 34.744)
	Treatment P-value [b]		0.19089
	Interaction P-value [c]		0.11082

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table AESISV.KM.S10.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Hyperglycemia	No. of Events (%)	6 (9.8)	1 (2.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.926 (0.593, 40.915)
	Treatment P-value [b]		0.09804
	Interaction P-value [c]		0.82434

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table AESISV.KM.S10.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Neuropathy	No. of Events (%)	4 (6.6)	1 (2.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.062 (0.342, 27.401)
	Treatment P-value [b]		0.30047
	Interaction P-value [c]		0.51282
Skin reactions	No. of Events (%)	9 (14.8)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00562
	Interaction P-value [c]		0.98499

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table AESISV.KM.S10.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Hyperglycemia	No. of Events (%)	13 (6.4)	2 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.603 (1.490, 29.261)
	Treatment P-value [b]		0.00424
	Interaction P-value [c]		0.82434

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table AESISV.KM.S10.SAF: Time to First Severe AESI (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Neuropathy	No. of Events (%)	9 (4.5)	6 (3.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.364 (0.485, 3.833)
	Treatment P-value [b]		0.56651
	Interaction P-value [c]		0.51282
Skin reactions	No. of Events (%)	33 (16.3)	2 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		17.539 (4.208, 73.098)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.98499

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

4.10.4 Schwerwiegend

Astellas: 7465-CL-0301
Table SAESI.KM.S1.SAF: Time to First Serious AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: <65 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=106)	Chemotherapy (N=103)
Skin reactions	No. of Events (%)	4 (3.8)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.04914
	Interaction P-value [c]		0.99991

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAESI.KM.S1.SAF: Time to First Serious AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 1, Level: >=65 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=190)	Chemotherapy (N=188)
Skin reactions	No. of Events (%)	10 (5.3)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00149
	Interaction P-value [c]		0.99991

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
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Astellas: 7465-CL-0301
Table SAESI.KM.S2.SAF: Time to First Serious AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: <75 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=245)	Chemotherapy (N=226)
Skin reactions	No. of Events (%)	11 (4.5)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00150
	Interaction P-value [c]		0.99993

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Date/time of run: 20APR2021 13:18
Analysis Plan: 15FEB2021 Confidential

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Table SAESI.KM.S2.SAF: Time to First Serious AESI (Months) (Safety Analysis Set)
Subgroup: Age Group 2, Level: >=75 years

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=51)	Chemotherapy (N=65)
Skin reactions	No. of Events (%)	3 (5.9)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.04648
	Interaction P-value [c]		0.99993

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table SAESI.KM.S3.SAF: Time to First Serious AESI (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Male

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=234)	Chemotherapy (N=219)
Skin reactions	No. of Events (%)	12 (5.1)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00076
	Interaction P-value [c]		0.99989

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Astellas: 7465-CL-0301
Table SAESI.KM.S3.SAF: Time to First Serious AESI (Months) (Safety Analysis Set)
Subgroup: Gender, Level: Female

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=62)	Chemotherapy (N=72)
Skin reactions	No. of Events (%)	2 (3.2)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.12316
	Interaction P-value [c]		0.99989

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

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Table SAESI.KM.S8.SAF: Time to First Serious AESI (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Upper Tract

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Skin reactions	No. of Events (%)	4 (4.2)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.03907
	Interaction P-value [c]		0.99995

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

Astellas: 7465-CL-0301
Table SAESI.KM.S8.SAF: Time to First Serious AESI (Months) (Safety Analysis Set)
Subgroup: Primary Site of Tumor, Level: Other

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=200)	Chemotherapy (N=189)
Skin reactions	No. of Events (%)	10 (5.0)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00204
	Interaction P-value [c]		0.99995

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table SAESI.KM.S9.SAF: Time to First Serious AESI (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: 1-2 lines

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Skin reactions	No. of Events (%)	11 (4.2)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00097
	Interaction P-value [c]		0.99990

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table SAESI.KM.S9.SAF: Time to First Serious AESI (Months) (Safety Analysis Set)
Subgroup: Prior Lines of Systemic Therapy, Level: >=3 lines

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Skin reactions	No. of Events (%)	3 (8.1)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.08515
	Interaction P-value [c]		0.99990

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Analysis Plan: 15FEB2021 Confidential

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Table SAESI.KM.S10.SAF: Time to First Serious AESI (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Responder

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Skin reactions	No. of Events (%)	2 (3.3)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.20389
	Interaction P-value [c]		0.99987

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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Table SAESI.KM.S10.SAF: Time to First Serious AESI (Months) (Safety Analysis Set)
Subgroup: Best Response to Prior CPI, Level: Non-responder

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Skin reactions	No. of Events (%)	12 (5.9)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00048
	Interaction P-value [c]		0.99987

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

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