Dossier zur Nutzenbewertung gemäß § 35a SGB V

Enfortumab Vedotin (PADCEV™)

Astellas Pharma GmbH

Anhang 4-G2

2. Datenschnitt vom 30.07.2021
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 (%)	76 (70.4)	84 (75.7)
	Median Survival Est. (Months) (95% CI)	12.29 (10.51, 16.46)	8.31 (7.10, 10.87)
	Hazard Ratio (95% CI)	0.762 (0.559, 1.040)	
	Treatment P-value [a]	0.10830	
	Interaction P-value [b]	0.79445	
6 Months	Patients at Risk, Survival Est. (95% CI)	84, 0.80 (0.71, 0.87)	69, 0.66 (0.56, 0.74)
12 Months	Patients at Risk, Survival Est. (95% CI)	54, 0.53 (0.43, 0.62)	38, 0.37 (0.28, 0.46)
18 Months	Patients at Risk, Survival Est. (95% CI)	34, 0.34 (0.25, 0.43)	32, 0.31 (0.23, 0.40)
24 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.25 (0.17, 0.35)	14, 0.20 (0.13, 0.29)
30 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.23 (0.14, 0.33)	1, 0.17 (0.10, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	131 (67.9)	153 (78.1)
	Median Survival Est. (Months) (95% CI)	12.91 (10.78, 16.30)	9.23 (8.44, 10.55)
	Hazard Ratio (95% CI)	0.724 (0.573, 0.915)	
	Treatment P-value [a]	0.00674	
	Interaction P-value [b]	0.79445	
6 Months	Patients at Risk, Survival Est. (95% CI)	142, 0.77 (0.70, 0.82)	134, 0.72 (0.65, 0.77)
12 Months	Patients at Risk, Survival Est. (95% CI)	96, 0.53 (0.46, 0.60)	73, 0.40 (0.33, 0.47)
18 Months	Patients at Risk, Survival Est. (95% CI)	72, 0.40 (0.33, 0.47)	46, 0.25 (0.19, 0.31)
24 Months	Patients at Risk, Survival Est. (95% CI)	29, 0.31 (0.25, 0.38)	18, 0.20 (0.14, 0.26)
30 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.20 (0.12, 0.29)	4, 0.13 (0.08, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	171 (68.7)	182 (76.2)
	Median Survival Est. (Months) (95% CI)	13.57 (11.07, 16.46)	8.94 (8.05, 10.58)
	Hazard Ratio (95% CI)	0.715 (0.580, 0.881)	
	Treatment P-value [a]	0.00175	
	Interaction P-value [b]	0.40514	
6 Months	Patients at Risk, Survival Est. (95% CI)	191, 0.79 (0.73, 0.83)	154, 0.68 (0.61, 0.73)
12 Months	Patients at Risk, Survival Est. (95% CI)	128, 0.54 (0.48, 0.60)	87, 0.39 (0.33, 0.45)
18 Months	Patients at Risk, Survival Est. (95% CI)	91, 0.39 (0.33, 0.45)	61, 0.27 (0.22, 0.33)
24 Months	Patients at Risk, Survival Est. (95% CI)	37, 0.30 (0.24, 0.36)	24, 0.20 (0.15, 0.26)
30 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.22 (0.15, 0.30)	3, 0.16 (0.11, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	36 (69.2)	55 (80.9)
	Median Survival Est. (Months) (95% CI)	10.09 (8.44, 15.18)	8.90 (7.52, 10.87)
	Hazard Ratio (95% CI)	0.872 (0.573, 1.329)	
	Treatment P-value [a]	0.58332	
	Interaction P-value [b]	0.40514	
6 Months	Patients at Risk, Survival Est. (95% CI)	35, 0.74 (0.59, 0.84)	49, 0.76 (0.63, 0.84)
12 Months	Patients at Risk, Survival Est. (95% CI)	22, 0.48 (0.33, 0.61)	24, 0.37 (0.26, 0.49)
18 Months	Patients at Risk, Survival Est. (95% CI)	15, 0.32 (0.20, 0.46)	17, 0.26 (0.16, 0.37)
24 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.24 (0.13, 0.38)	8, 0.19 (0.10, 0.30)
30 Months	Patients at Risk, Survival Est. (95% CI)	0	2, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	159 (66.8)	187 (80.6)
	Median Survival Est. (Months) (95% CI)	13.47 (11.01, 17.02)	8.87 (8.05, 10.02)
	Hazard Ratio (95% CI)	0.638 (0.516, 0.788)	
	Treatment P-value [a]	0.00002	
	Interaction P-value [b]	0.00634	
6 Months	Patients at Risk, Survival Est. (95% CI)	181, 0.80 (0.74, 0.84)	151, 0.68 (0.62, 0.74)
12 Months	Patients at Risk, Survival Est. (95% CI)	121, 0.55 (0.48, 0.61)	78, 0.36 (0.30, 0.42)
18 Months	Patients at Risk, Survival Est. (95% CI)	87, 0.40 (0.34, 0.46)	52, 0.24 (0.18, 0.30)
24 Months	Patients at Risk, Survival Est. (95% CI)	38, 0.31 (0.25, 0.38)	22, 0.17 (0.12, 0.22)
30 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.22 (0.15, 0.31)	2, 0.11 (0.07, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	48 (76.2)	50 (66.7)
	Median Survival Est. (Months) (95% CI)	11.40 (8.28, 14.92)	10.68 (7.62, 17.25)
	Hazard Ratio (95% CI)	1.194 (0.803, 1.776)	
	Treatment P-value [a]	0.36672	
	Interaction P-value [b]	0.00634	
6 Months	Patients at Risk, Survival Est. (95% CI)	45, 0.71 (0.59, 0.81)	52, 0.74 (0.62, 0.82)
12 Months	Patients at Risk, Survival Est. (95% CI)	29, 0.47 (0.34, 0.59)	33, 0.48 (0.36, 0.59)
18 Months	Patients at Risk, Survival Est. (95% CI)	19, 0.31 (0.20, 0.43)	26, 0.38 (0.27, 0.49)
24 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.20 (0.10, 0.34)	10, 0.29 (0.18, 0.41)
30 Months	Patients at Risk, Survival Est. (95% CI)	0	3, 0.23 (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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	92 (73.0)	104 (80.6)
	Median Survival Est. (Months) (95% CI)	12.29 (9.36, 14.92)	8.74 (7.36, 10.38)
	Hazard Ratio (95% CI)	0.744 (0.562, 0.986)	
	Treatment P-value [a]	0.03736	
	Interaction P-value [b]	0.57325	
6 Months	Patients at Risk, Survival Est. (95% CI)	92, 0.74 (0.66, 0.81)	81, 0.65 (0.56, 0.73)
12 Months	Patients at Risk, Survival Est. (95% CI)	63, 0.52 (0.43, 0.60)	46, 0.37 (0.29, 0.45)
18 Months	Patients at Risk, Survival Est. (95% CI)	42, 0.34 (0.26, 0.43)	28, 0.22 (0.16, 0.30)
24 Months	Patients at Risk, Survival Est. (95% CI)	14, 0.25 (0.17, 0.33)	12, 0.18 (0.12, 0.25)
30 Months	Patients at Risk, Survival Est. (95% CI)	0	2, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	31 (72.1)	30 (68.2)
	Median Survival Est. (Months) (95% CI)	10.45 (7.52, 20.27)	8.94 (6.05, 18.79)
	Hazard Ratio (95% CI)	0.925 (0.560, 1.529)	
	Treatment P-value [a]	0.66772	
	Interaction P-value [b]	0.57325	
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)	18, 0.45 (0.30, 0.60)	17, 0.45 (0.29, 0.59)
18 Months	Patients at Risk, Survival Est. (95% CI)	15, 0.38 (0.23, 0.52)	14, 0.37 (0.22, 0.51)
24 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.35 (0.21, 0.50)	6, 0.22 (0.11, 0.37)
30 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.10 (0.01, 0.30)	1, 0.22 (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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	84 (63.6)	103 (76.9)
	Median Survival Est. (Months) (95% CI)	14.32 (11.40, 18.04)	8.94 (8.05, 10.87)
	Hazard Ratio (95% CI)	0.678 (0.508, 0.905)	
	Treatment P-value [a]	0.00640	
	Interaction P-value [b]	0.57325	
6 Months	Patients at Risk, Survival Est. (95% CI)	104, 0.82 (0.74, 0.88)	95, 0.74 (0.66, 0.81)
12 Months	Patients at Risk, Survival Est. (95% CI)	69, 0.57 (0.48, 0.65)	48, 0.39 (0.30, 0.47)
18 Months	Patients at Risk, Survival Est. (95% CI)	49, 0.42 (0.33, 0.50)	36, 0.29 (0.21, 0.37)
24 Months	Patients at Risk, Survival Est. (95% CI)	15, 0.31 (0.22, 0.41)	14, 0.22 (0.15, 0.29)
30 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.26 (0.16, 0.36)	2, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	71 (59.2)	81 (65.3)
	Median Survival Est. (Months) (95% CI)	17.25 (14.32, 21.75)	13.11 (10.15, 17.61)
	Hazard Ratio (95% CI)	0.794 (0.578, 1.093)	
	Treatment P-value [a]	0.13194	
	Interaction P-value [b]	0.44735	
6 Months	Patients at Risk, Survival Est. (95% CI)	103, 0.87 (0.80, 0.92)	105, 0.89 (0.82, 0.94)
12 Months	Patients at Risk, Survival Est. (95% CI)	74, 0.64 (0.55, 0.72)	61, 0.53 (0.44, 0.62)
18 Months	Patients at Risk, Survival Est. (95% CI)	55, 0.48 (0.39, 0.57)	47, 0.41 (0.32, 0.50)
24 Months	Patients at Risk, Survival Est. (95% CI)	23, 0.39 (0.30, 0.48)	18, 0.31 (0.22, 0.40)
30 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.36 (0.25, 0.46)	4, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	136 (75.1)	156 (85.2)
	Median Survival Est. (Months) (95% CI)	10.71 (8.48, 12.81)	6.97 (5.85, 8.28)
	Hazard Ratio (95% CI)	0.682 (0.542, 0.859)	
	Treatment P-value [a]	0.00193	
	Interaction P-value [b]	0.44735	
6 Months	Patients at Risk, Survival Est. (95% CI)	123, 0.72 (0.64, 0.78)	98, 0.56 (0.49, 0.63)
12 Months	Patients at Risk, Survival Est. (95% CI)	76, 0.45 (0.38, 0.53)	50, 0.29 (0.23, 0.36)
18 Months	Patients at Risk, Survival Est. (95% CI)	51, 0.31 (0.24, 0.38)	31, 0.18 (0.13, 0.24)
24 Months	Patients at Risk, Survival Est. (95% CI)	18, 0.23 (0.17, 0.30)	14, 0.13 (0.08, 0.18)
30 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.10 (0.03, 0.20)	1, 0.07 (0.03, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	71 (76.3)	82 (86.3)
	Median Survival Est. (Months) (95% CI)	9.36 (6.80, 11.04)	5.95 (4.93, 7.23)
	Hazard Ratio (95% CI)	0.631 (0.459, 0.868)	
	Treatment P-value [a]	0.00921	
	Interaction P-value [b]	0.32722	
6 Months	Patients at Risk, Survival Est. (95% CI)	54, 0.63 (0.52, 0.72)	43, 0.50 (0.39, 0.59)
12 Months	Patients at Risk, Survival Est. (95% CI)	32, 0.38 (0.28, 0.48)	18, 0.21 (0.13, 0.30)
18 Months	Patients at Risk, Survival Est. (95% CI)	21, 0.26 (0.17, 0.36)	10, 0.12 (0.06, 0.20)
24 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.19 (0.11, 0.28)	4, 0.08 (0.03, 0.15)
30 Months	Patients at Risk, Survival Est. (95% CI)	0	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	136 (65.4)	155 (73.1)
	Median Survival Est. (Months) (95% CI)	15.11 (12.88, 18.07)	10.55 (9.17, 13.70)
	Hazard Ratio (95% CI)	0.768 (0.610, 0.967)	
	Treatment P-value [a]	0.02227	
	Interaction P-value [b]	0.32722	
6 Months	Patients at Risk, Survival Est. (95% CI)	172, 0.84 (0.79, 0.89)	160, 0.78 (0.72, 0.83)
12 Months	Patients at Risk, Survival Est. (95% CI)	118, 0.59 (0.52, 0.66)	93, 0.46 (0.39, 0.53)
18 Months	Patients at Risk, Survival Est. (95% CI)	85, 0.43 (0.36, 0.50)	68, 0.34 (0.27, 0.40)
24 Months	Patients at Risk, Survival Est. (95% CI)	34, 0.34 (0.27, 0.41)	28, 0.25 (0.19, 0.31)
30 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.25 (0.17, 0.34)	4, 0.19 (0.13, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: Paclitaxel

Time Point	Statistics	Enfortumab Vedotin (N=141)	Chemotherapy (N=112)
Overall	No. of Events (%)	100 (70.9)	83 (74.1)
	Median Survival Est. (Months) (95% CI)	13.17 (10.81, 16.59)	9.23 (8.15, 11.56)
	Hazard Ratio (95% CI)	0.783 (0.585, 1.048)	
	Treatment P-value [a]	0.09302	
	Interaction P-value [b]	0.82084	
6 Months	Patients at Risk, Survival Est. (95% CI)	106, 0.79 (0.71, 0.85)	70, 0.66 (0.56, 0.74)
12 Months	Patients at Risk, Survival Est. (95% CI)	68, 0.52 (0.43, 0.60)	40, 0.40 (0.30, 0.49)
18 Months	Patients at Risk, Survival Est. (95% CI)	48, 0.37 (0.29, 0.45)	28, 0.28 (0.19, 0.37)
24 Months	Patients at Risk, Survival Est. (95% CI)	20, 0.26 (0.18, 0.34)	10, 0.22 (0.14, 0.31)
30 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.21 (0.13, 0.29)	2, 0.17 (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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	59 (67.8)	94 (80.3)
	Median Survival Est. (Months) (95% CI)	13.47 (9.86, 18.07)	8.44 (7.52, 10.58)
	Hazard Ratio (95% CI)	0.681 (0.492, 0.943)	
	Treatment P-value [a]	0.01441	
	Interaction P-value [b]	0.82084	
6 Months	Patients at Risk, Survival Est. (95% CI)	67, 0.79 (0.69, 0.86)	82, 0.73 (0.64, 0.80)
12 Months	Patients at Risk, Survival Est. (95% CI)	44, 0.54 (0.43, 0.64)	41, 0.37 (0.28, 0.45)
18 Months	Patients at Risk, Survival Est. (95% CI)	32, 0.41 (0.30, 0.51)	31, 0.28 (0.20, 0.36)
24 Months	Patients at Risk, Survival Est. (95% CI)	14, 0.33 (0.23, 0.44)	15, 0.19 (0.12, 0.27)
30 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.16 (0.06, 0.31)	2, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	48 (65.8)	60 (76.9)
	Median Survival Est. (Months) (95% CI)	12.81 (8.38, 17.18)	9.46 (7.85, 13.11)
	Hazard Ratio (95% CI)	0.741 (0.507, 1.083)	
	Treatment P-value [a]	0.12885	
	Interaction P-value [b]	0.82084	
6 Months	Patients at Risk, Survival Est. (95% CI)	53, 0.75 (0.63, 0.83)	51, 0.69 (0.58, 0.78)
12 Months	Patients at Risk, Survival Est. (95% CI)	38, 0.54 (0.42, 0.65)	30, 0.41 (0.30, 0.52)
18 Months	Patients at Risk, Survival Est. (95% CI)	26, 0.37 (0.26, 0.48)	19, 0.26 (0.17, 0.36)
24 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.32 (0.22, 0.43)	7, 0.20 (0.11, 0.30)
30 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	62 (63.3)	76 (71.0)
	Median Survival Est. (Months) (95% CI)	13.57 (10.48, 18.07)	10.74 (8.05, 14.06)
	Hazard Ratio (95% CI)	0.800 (0.572, 1.119)	
	Treatment P-value [a]	0.19941	
	Interaction P-value [b]	0.51136	
6 Months	Patients at Risk, Survival Est. (95% CI)	73, 0.78 (0.68, 0.85)	76, 0.75 (0.65, 0.82)
12 Months	Patients at Risk, Survival Est. (95% CI)	50, 0.54 (0.44, 0.64)	46, 0.46 (0.36, 0.55)
18 Months	Patients at Risk, Survival Est. (95% CI)	37, 0.42 (0.32, 0.52)	34, 0.34 (0.25, 0.43)
24 Months	Patients at Risk, Survival Est. (95% CI)	15, 0.33 (0.23, 0.43)	14, 0.27 (0.18, 0.36)
30 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.30 (0.20, 0.41)	2, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	145 (71.4)	161 (80.5)
	Median Survival Est. (Months) (95% CI)	12.88 (10.58, 14.78)	8.74 (7.62, 9.46)
	Hazard Ratio (95% CI)	0.699 (0.558, 0.875)	
	Treatment P-value [a]	0.00151	
	Interaction P-value [b]	0.51136	
6 Months	Patients at Risk, Survival Est. (95% CI)	153, 0.78 (0.72, 0.83)	127, 0.67 (0.59, 0.73)
12 Months	Patients at Risk, Survival Est. (95% CI)	100, 0.52 (0.45, 0.59)	65, 0.35 (0.28, 0.42)
18 Months	Patients at Risk, Survival Est. (95% CI)	69, 0.36 (0.29, 0.43)	44, 0.24 (0.18, 0.30)
24 Months	Patients at Risk, Survival Est. (95% CI)	26, 0.28 (0.21, 0.34)	18, 0.16 (0.11, 0.22)
30 Months	Patients at Risk, Survival Est. (95% CI)	2, 0.16 (0.09, 0.26)	3, 0.10 (0.05, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	181 (69.1)	208 (77.0)
	Median Survival Est. (Months) (95% CI)	12.91 (11.04, 14.92)	8.94 (8.05, 10.25)
	Hazard Ratio (95% CI)	0.730 (0.598, 0.891)	
	Treatment P-value [a]	0.00177	
	Interaction P-value [b]	0.77084	
6 Months	Patients at Risk, Survival Est. (95% CI)	196, 0.78 (0.72, 0.82)	177, 0.69 (0.63, 0.75)
12 Months	Patients at Risk, Survival Est. (95% CI)	132, 0.54 (0.47, 0.59)	98, 0.39 (0.33, 0.45)
18 Months	Patients at Risk, Survival Est. (95% CI)	90, 0.37 (0.31, 0.43)	68, 0.27 (0.22, 0.33)
24 Months	Patients at Risk, Survival Est. (95% CI)	37, 0.29 (0.23, 0.34)	27, 0.20 (0.15, 0.25)
30 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.19 (0.12, 0.28)	4, 0.14 (0.09, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	26 (66.7)	29 (78.4)
	Median Survival Est. (Months) (95% CI)	10.71 (7.52, 24.61)	9.33 (7.10, 13.27)
	Hazard Ratio (95% CI)	0.794 (0.467, 1.349)	
	Treatment P-value [a]	0.36213	
	Interaction P-value [b]	0.77084	
6 Months	Patients at Risk, Survival Est. (95% CI)	30, 0.79 (0.63, 0.89)	26, 0.70 (0.53, 0.82)
12 Months	Patients at Risk, Survival Est. (95% CI)	18, 0.49 (0.33, 0.64)	13, 0.37 (0.22, 0.52)
18 Months	Patients at Risk, Survival Est. (95% CI)	16, 0.44 (0.28, 0.59)	10, 0.29 (0.15, 0.44)
24 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.35 (0.21, 0.51)	5, 0.21 (0.09, 0.37)
30 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.27 (0.10, 0.46)	1, 0.17 (0.06, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	33 (54.1)	39 (78.0)
	Median Survival Est. (Months) (95% CI)	18.69 (13.27, NC)	11.07 (8.41, 18.10)
	Hazard Ratio (95% CI)	0.570 (0.359, 0.907)	
	Treatment P-value [a]	0.01566	
	Interaction P-value [b]	0.20690	
6 Months	Patients at Risk, Survival Est. (95% CI)	51, 0.85 (0.73, 0.92)	39, 0.80 (0.65, 0.88)
12 Months	Patients at Risk, Survival Est. (95% CI)	42, 0.70 (0.57, 0.80)	23, 0.47 (0.33, 0.60)
18 Months	Patients at Risk, Survival Est. (95% CI)	31, 0.55 (0.41, 0.66)	19, 0.39 (0.25, 0.52)
24 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.42 (0.29, 0.55)	7, 0.25 (0.14, 0.38)
30 Months	Patients at Risk, Survival Est. (95% CI)	0	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	150 (72.5)	165 (76.7)
	Median Survival Est. (Months) (95% CI)	11.63 (10.15, 14.32)	8.94 (8.05, 10.48)
	Hazard Ratio (95% CI)	0.794 (0.636, 0.990)	
	Treatment P-value [a]	0.04071	
	Interaction P-value [b]	0.20690	
6 Months	Patients at Risk, Survival Est. (95% CI)	152, 0.77 (0.70, 0.82)	138, 0.68 (0.61, 0.74)
12 Months	Patients at Risk, Survival Est. (95% CI)	93, 0.48 (0.41, 0.55)	74, 0.37 (0.31, 0.44)
18 Months	Patients at Risk, Survival Est. (95% CI)	65, 0.34 (0.27, 0.40)	49, 0.25 (0.19, 0.31)
24 Months	Patients at Risk, Survival Est. (95% CI)	28, 0.26 (0.20, 0.33)	20, 0.19 (0.14, 0.25)
30 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.17 (0.10, 0.25)	4, 0.13 (0.08, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	82 (75.9)	84 (75.7)
	Median Survival Est. (Months) (95% CI)	5.45 (3.94, 6.34)	3.55 (2.37, 3.84)
	Hazard Ratio (95% CI)	0.703 (0.518, 0.954)	
	Treatment P-value [a]	0.03130	
	Interaction P-value [b]	0.56542	
6 Months	Patients at Risk, Survival Est. (95% CI)	41, 0.43 (0.33, 0.53)	25, 0.28 (0.19, 0.37)
12 Months	Patients at Risk, Survival Est. (95% CI)	20, 0.22 (0.14, 0.31)	7, 0.10 (0.05, 0.18)
18 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.16 (0.09, 0.24)	6, 0.09 (0.04, 0.16)
24 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.14 (0.08, 0.22)	4, 0.09 (0.04, 0.16)
30 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.14 (0.08, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	149 (77.2)	164 (83.7)
	Median Survival Est. (Months) (95% CI)	5.65 (5.32, 7.20)	3.84 (3.52, 4.90)
	Hazard Ratio (95% CI)	0.630 (0.503, 0.787)	
	Treatment P-value [a]	0.00002	
	Interaction P-value [b]	0.56542	
6 Months	Patients at Risk, Survival Est. (95% CI)	77, 0.45 (0.38, 0.53)	51, 0.30 (0.23, 0.37)
12 Months	Patients at Risk, Survival Est. (95% CI)	45, 0.27 (0.20, 0.33)	14, 0.10 (0.06, 0.15)
18 Months	Patients at Risk, Survival Est. (95% CI)	26, 0.17 (0.11, 0.23)	8, 0.07 (0.04, 0.12)
24 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.12 (0.07, 0.19)	3, 0.04 (0.02, 0.09)
30 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.04 (0.02, 0.09)

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	193 (77.5)	193 (80.8)
	Median Survival Est. (Months) (95% CI)	5.62 (5.32, 6.47)	3.68 (3.32, 3.94)
	Hazard Ratio (95% CI)	0.626 (0.512, 0.765)	
	Treatment P-value [a]	<.00001	
	Interaction P-value [b]	0.27488	
6 Months	Patients at Risk, Survival Est. (95% CI)	101, 0.45 (0.39, 0.52)	59, 0.29 (0.23, 0.35)
12 Months	Patients at Risk, Survival Est. (95% CI)	59, 0.27 (0.21, 0.33)	16, 0.10 (0.06, 0.14)
18 Months	Patients at Risk, Survival Est. (95% CI)	34, 0.17 (0.12, 0.22)	13, 0.08 (0.04, 0.12)
24 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.13 (0.09, 0.19)	7, 0.07 (0.04, 0.11)
30 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.13 (0.09, 0.19)	1, 0.07 (0.04, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	38 (73.1)	55 (80.9)
	Median Survival Est. (Months) (95% CI)	5.42 (3.71, 7.33)	3.84 (3.52, 5.62)
	Hazard Ratio (95% CI)	0.808 (0.534, 1.222)	
	Treatment P-value [a]	0.31234	
	Interaction P-value [b]	0.27488	
6 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.41 (0.26, 0.55)	17, 0.31 (0.20, 0.43)
12 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.14 (0.06, 0.27)	5, 0.11 (0.04, 0.20)
18 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.11 (0.04, 0.23)	1, 0.06 (0.01, 0.15)
24 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.11 (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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	179 (75.2)	191 (82.3)
	Median Survival Est. (Months) (95% CI)	5.65 (5.32, 7.16)	3.68 (3.42, 3.84)
	Hazard Ratio (95% CI)	0.589 (0.479, 0.724)	
	Treatment P-value [a]	<.00001	
	Interaction P-value [b]	0.04260	
6 Months	Patients at Risk, Survival Est. (95% CI)	98, 0.47 (0.40, 0.53)	52, 0.26 (0.20, 0.32)
12 Months	Patients at Risk, Survival Est. (95% CI)	56, 0.27 (0.21, 0.33)	12, 0.08 (0.05, 0.13)
18 Months	Patients at Risk, Survival Est. (95% CI)	33, 0.18 (0.13, 0.23)	9, 0.06 (0.03, 0.10)
24 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.14 (0.09, 0.20)	4, 0.05 (0.02, 0.09)
30 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.14 (0.09, 0.20)	0

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	52 (82.5)	57 (76.0)
	Median Survival Est. (Months) (95% CI)	5.39 (3.75, 5.78)	3.94 (2.99, 7.29)
	Hazard Ratio (95% CI)	0.918 (0.630, 1.337)	
	Treatment P-value [a]	0.63120	
	Interaction P-value [b]	0.04260	
6 Months	Patients at Risk, Survival Est. (95% CI)	20, 0.36 (0.24, 0.48)	24, 0.39 (0.27, 0.50)
12 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.16 (0.08, 0.27)	9, 0.15 (0.08, 0.25)
18 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.10 (0.04, 0.20)	5, 0.12 (0.05, 0.21)
24 Months	Patients at Risk, Survival Est. (95% CI)	0	3, 0.10 (0.04, 0.19)
30 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.10 (0.04, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Western Europe

Time Point	Statistics	Enfortumab Vedotin (N=126)	Chemotherapy (N=129)
Overall	No. of Events (%)	102 (81.0)	101 (78.3)
	Median Survival Est. (Months) (95% CI)	5.55 (3.91, 7.16)	3.75 (3.02, 5.13)
	Hazard Ratio (95% CI)	0.726 (0.551, 0.956)	
	Treatment P-value [a]	0.02465	
	Interaction P-value [b]	0.60313	
6 Months	Patients at Risk, Survival Est. (95% CI)	52, 0.45 (0.36, 0.54)	32, 0.28 (0.20, 0.37)
12 Months	Patients at Risk, Survival Est. (95% CI)	27, 0.23 (0.16, 0.31)	13, 0.14 (0.08, 0.21)
18 Months	Patients at Risk, Survival Est. (95% CI)	16, 0.14 (0.09, 0.21)	9, 0.12 (0.06, 0.19)
24 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.12 (0.07, 0.19)	5, 0.09 (0.04, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	32 (74.4)	35 (79.5)
	Median Survival Est. (Months) (95% CI)	5.62 (3.45, 7.46)	3.35 (2.07, 5.62)
	Hazard Ratio (95% CI)	0.634 (0.393, 1.026)	
	Treatment P-value [a]	0.05920	
	Interaction P-value [b]	0.60313	
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)	9, 0.24 (0.12, 0.39)	2, 0.06 (0.01, 0.17)
18 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.15 (0.05, 0.29)	1, 0.03 (0.00, 0.13)
24 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.10 (0.02, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Rest of the World

Time Point	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=134)
Overall	No. of Events (%)	97 (73.5)	112 (83.6)
	Median Survival Est. (Months) (95% CI)	5.55 (5.32, 7.20)	3.71 (3.52, 5.39)
	Hazard Ratio (95% CI)	0.596 (0.453, 0.784)	
	Treatment P-value [a]	0.00015	
	Interaction P-value [b]	0.60313	
6 Months	Patients at Risk, Survival Est. (95% CI)	50, 0.45 (0.36, 0.53)	33, 0.29 (0.21, 0.37)
12 Months	Patients at Risk, Survival Est. (95% CI)	29, 0.27 (0.19, 0.35)	6, 0.07 (0.03, 0.13)
18 Months	Patients at Risk, Survival Est. (95% CI)	18, 0.19 (0.12, 0.26)	4, 0.04 (0.02, 0.10)
24 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.16 (0.09, 0.24)	2, 0.03 (0.01, 0.09)
30 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.16 (0.09, 0.24)	1, 0.03 (0.01, 0.09)

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	85 (70.8)	98 (79.0)
	Median Survival Est. (Months) (95% CI)	7.20 (5.55, 8.41)	4.90 (3.71, 5.59)
	Hazard Ratio (95% CI)	0.625 (0.467, 0.836)	
	Treatment P-value [a]	0.00114	
	Interaction P-value [b]	0.75571	
6 Months	Patients at Risk, Survival Est. (95% CI)	57, 0.52 (0.43, 0.61)	37, 0.35 (0.26, 0.44)
12 Months	Patients at Risk, Survival Est. (95% CI)	34, 0.32 (0.23, 0.41)	13, 0.13 (0.07, 0.20)
18 Months	Patients at Risk, Survival Est. (95% CI)	23, 0.25 (0.17, 0.33)	9, 0.09 (0.04, 0.15)
24 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.21 (0.13, 0.29)	6, 0.08 (0.04, 0.14)
30 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.21 (0.13, 0.29)	1, 0.08 (0.04, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	146 (80.7)	150 (82.0)
	Median Survival Est. (Months) (95% CI)	5.39 (3.94, 5.65)	3.35 (2.23, 3.78)
	Hazard Ratio (95% CI)	0.662 (0.527, 0.833)	
	Treatment P-value [a]	0.00068	
	Interaction P-value [b]	0.75571	
6 Months	Patients at Risk, Survival Est. (95% CI)	61, 0.39 (0.32, 0.47)	39, 0.25 (0.19, 0.32)
12 Months	Patients at Risk, Survival Est. (95% CI)	31, 0.20 (0.14, 0.27)	8, 0.08 (0.04, 0.13)
18 Months	Patients at Risk, Survival Est. (95% CI)	15, 0.10 (0.06, 0.16)	5, 0.07 (0.03, 0.12)
24 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.08 (0.04, 0.14)	1, 0.04 (0.01, 0.09)

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	79 (84.9)	81 (85.3)
	Median Survival Est. (Months) (95% CI)	4.14 (3.71, 5.55)	2.63 (2.07, 3.55)
	Hazard Ratio (95% CI)	0.603 (0.441, 0.824)	
	Treatment P-value [a]	0.00198	
	Interaction P-value [b]	0.64424	
6 Months	Patients at Risk, Survival Est. (95% CI)	29, 0.35 (0.25, 0.45)	12, 0.14 (0.08, 0.23)
12 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.16 (0.09, 0.24)	4, 0.05 (0.02, 0.12)
18 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.06 (0.02, 0.13)	2, 0.04 (0.01, 0.10)
24 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.04 (0.01, 0.11)	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	152 (73.1)	167 (78.8)
	Median Survival Est. (Months) (95% CI)	5.78 (5.49, 7.23)	4.14 (3.68, 5.55)
	Hazard Ratio (95% CI)	0.660 (0.529, 0.823)	
	Treatment P-value [a]	0.00022	
	Interaction P-value [b]	0.64424	
6 Months	Patients at Risk, Survival Est. (95% CI)	89, 0.49 (0.41, 0.56)	64, 0.36 (0.29, 0.43)
12 Months	Patients at Risk, Survival Est. (95% CI)	52, 0.29 (0.22, 0.36)	17, 0.12 (0.07, 0.17)
18 Months	Patients at Risk, Survival Est. (95% CI)	34, 0.21 (0.15, 0.27)	12, 0.09 (0.05, 0.14)
24 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.17 (0.11, 0.23)	6, 0.07 (0.04, 0.12)
30 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.17 (0.11, 0.23)	1, 0.07 (0.04, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	112 (79.4)	98 (87.5)
	Median Survival Est. (Months) (95% CI)	5.55 (4.44, 7.20)	3.65 (3.35, 5.13)
	Hazard Ratio (95% CI)	0.655 (0.499, 0.860)	
	Treatment P-value [a]	0.00159	
	Interaction P-value [b]	0.31665	
6 Months	Patients at Risk, Survival Est. (95% CI)	55, 0.45 (0.36, 0.53)	29, 0.29 (0.20, 0.38)
12 Months	Patients at Risk, Survival Est. (95% CI)	30, 0.24 (0.17, 0.32)	9, 0.10 (0.05, 0.16)
18 Months	Patients at Risk, Survival Est. (95% CI)	15, 0.14 (0.08, 0.21)	6, 0.06 (0.03, 0.12)
24 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.10 (0.05, 0.17)	2, 0.04 (0.01, 0.10)
30 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.10 (0.05, 0.17)	1, 0.04 (0.01, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	64 (73.6)	91 (77.8)
	Median Survival Est. (Months) (95% CI)	5.68 (3.94, 7.46)	3.25 (2.20, 3.84)
	Hazard Ratio (95% CI)	0.547 (0.396, 0.755)	
	Treatment P-value [a]	0.00037	
	Interaction P-value [b]	0.31665	
6 Months	Patients at Risk, Survival Est. (95% CI)	36, 0.48 (0.37, 0.59)	24, 0.27 (0.18, 0.36)
12 Months	Patients at Risk, Survival Est. (95% CI)	19, 0.26 (0.17, 0.36)	4, 0.06 (0.02, 0.12)
18 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.19 (0.11, 0.28)	3, 0.04 (0.01, 0.11)
24 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.13 (0.06, 0.24)	2, 0.04 (0.01, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	55 (75.3)	59 (75.6)
	Median Survival Est. (Months) (95% CI)	5.55 (3.84, 6.77)	4.14 (3.68, 5.62)
	Hazard Ratio (95% CI)	0.797 (0.552, 1.152)	
	Treatment P-value [a]	0.22977	
	Interaction P-value [b]	0.31665	
6 Months	Patients at Risk, Survival Est. (95% CI)	27, 0.41 (0.29, 0.52)	23, 0.33 (0.23, 0.44)
12 Months	Patients at Risk, Survival Est. (95% CI)	16, 0.24 (0.15, 0.35)	8, 0.15 (0.08, 0.25)
18 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.18 (0.10, 0.28)	5, 0.13 (0.06, 0.23)
24 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.18 (0.10, 0.28)	3, 0.11 (0.04, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	71 (72.4)	81 (75.7)
	Median Survival Est. (Months) (95% CI)	5.62 (5.32, 7.49)	3.78 (2.23, 5.39)
	Hazard Ratio (95% CI)	0.696 (0.506, 0.958)	
	Treatment P-value [a]	0.03369	
	Interaction P-value [b]	0.58339	
6 Months	Patients at Risk, Survival Est. (95% CI)	42, 0.49 (0.38, 0.58)	31, 0.34 (0.25, 0.44)
12 Months	Patients at Risk, Survival Est. (95% CI)	24, 0.28 (0.19, 0.38)	12, 0.16 (0.09, 0.25)
18 Months	Patients at Risk, Survival Est. (95% CI)	15, 0.21 (0.13, 0.30)	9, 0.13 (0.07, 0.22)
24 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.17 (0.10, 0.27)	5, 0.10 (0.05, 0.18)
30 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.17 (0.10, 0.27)	1, 0.10 (0.05, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Other

Time Point	Statistics	Enfortumab Vedotin (N=203)	Chemotherapy (N=200)
Overall	No. of Events (%)	160 (78.8)	167 (83.5)
	Median Survival Est. (Months) (95% CI)	5.55 (4.44, 5.82)	3.68 (3.38, 3.94)
	Hazard Ratio (95% CI)	0.625 (0.502, 0.778)	
	Treatment P-value [a]	0.00001	
	Interaction P-value [b]	0.58339	
6 Months	Patients at Risk, Survival Est. (95% CI)	76, 0.43 (0.36, 0.50)	45, 0.26 (0.20, 0.33)
12 Months	Patients at Risk, Survival Est. (95% CI)	41, 0.23 (0.17, 0.29)	9, 0.06 (0.03, 0.11)
18 Months	Patients at Risk, Survival Est. (95% CI)	23, 0.14 (0.09, 0.20)	5, 0.04 (0.02, 0.08)
24 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.11 (0.06, 0.17)	2, 0.03 (0.01, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	200 (76.3)	217 (80.4)
	Median Survival Est. (Months) (95% CI)	5.55 (5.32, 6.28)	3.75 (3.52, 4.04)
	Hazard Ratio (95% CI)	0.648 (0.534, 0.787)	
	Treatment P-value [a]	0.00001	
	Interaction P-value [b]	0.80754	
6 Months	Patients at Risk, Survival Est. (95% CI)	103, 0.45 (0.38, 0.51)	67, 0.29 (0.23, 0.35)
12 Months	Patients at Risk, Survival Est. (95% CI)	57, 0.25 (0.20, 0.31)	20, 0.10 (0.07, 0.15)
18 Months	Patients at Risk, Survival Est. (95% CI)	35, 0.17 (0.12, 0.22)	13, 0.08 (0.05, 0.12)
24 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.14 (0.10, 0.19)	6, 0.06 (0.03, 0.10)
30 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.14 (0.10, 0.19)	1, 0.06 (0.03, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: >=3 lines

Time Point	Statistics	Enfortumab Vedotin (N=39)	Chemotherapy (N=37)
Overall	No. of Events (%)	31 (79.5)	31 (83.8)
	Median Survival Est. (Months) (95% CI)	5.55 (3.71, 7.46)	3.61 (2.10, 5.68)
	Hazard Ratio (95% CI)	0.693 (0.421, 1.140)	
	Treatment P-value [a]	0.11012	
	Interaction P-value [b]	0.80754	
6 Months	Patients at Risk, Survival Est. (95% CI)	15, 0.45 (0.28, 0.61)	9, 0.29 (0.15, 0.45)
12 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.24 (0.11, 0.39)	1, 0.04 (0.00, 0.17)
18 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.10 (0.03, 0.24)	1, 0.04 (0.00, 0.17)
24 Months	Patients at Risk, Survival Est. (95% CI)	0	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Responder

Time Point	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=50)
Overall	No. of Events (%)	42 (68.9)	39 (78.0)
	Median Survival Est. (Months) (95% CI)	7.52 (5.78, 11.10)	5.39 (3.25, 7.36)
	Hazard Ratio (95% CI)	0.498 (0.321, 0.772)	
	Treatment P-value [a]	0.00052	
	Interaction P-value [b]	0.16210	
6 Months	Patients at Risk, Survival Est. (95% CI)	33, 0.61 (0.47, 0.72)	14, 0.36 (0.22, 0.50)
12 Months	Patients at Risk, Survival Est. (95% CI)	20, 0.37 (0.24, 0.49)	2, 0.06 (0.01, 0.16)
18 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.27 (0.16, 0.39)	1, 0.03 (0.00, 0.12)
24 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.22 (0.12, 0.34)	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	163 (78.7)	173 (80.5)
	Median Survival Est. (Months) (95% CI)	5.42 (4.44, 5.65)	3.65 (3.35, 3.84)
	Hazard Ratio (95% CI)	0.704 (0.568, 0.873)	
	Treatment P-value [a]	0.00179	
	Interaction P-value [b]	0.16210	
6 Months	Patients at Risk, Survival Est. (95% CI)	73, 0.41 (0.33, 0.47)	51, 0.28 (0.22, 0.35)
12 Months	Patients at Risk, Survival Est. (95% CI)	39, 0.22 (0.16, 0.28)	17, 0.11 (0.07, 0.16)
18 Months	Patients at Risk, Survival Est. (95% CI)	21, 0.13 (0.09, 0.19)	11, 0.08 (0.05, 0.13)
24 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.11 (0.06, 0.17)	4, 0.06 (0.03, 0.10)
30 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.11 (0.06, 0.17)	1, 0.06 (0.03, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	86 (79.6)	85 (76.6)
	Median Survival Est. (Months) (95% CI)	5.45 (4.44, 6.34)	3.55 (2.37, 3.84)
	Hazard Ratio (95% CI)	0.709 (0.525, 0.957)	
	Treatment P-value [a]	0.03123	
	Interaction P-value [b]	0.57505	
6 Months	Patients at Risk, Survival Est. (95% CI)	43, 0.43 (0.34, 0.53)	25, 0.28 (0.19, 0.37)
12 Months	Patients at Risk, Survival Est. (95% CI)	22, 0.22 (0.15, 0.31)	8, 0.11 (0.05, 0.18)
18 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.16 (0.09, 0.24)	7, 0.09 (0.04, 0.17)
24 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.13 (0.07, 0.21)	4, 0.08 (0.03, 0.15)
30 Months	Patients at Risk, Survival Est. (95% CI)	1, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	152 (78.8)	171 (87.2)
	Median Survival Est. (Months) (95% CI)	5.65 (5.32, 7.20)	3.84 (3.61, 5.39)
	Hazard Ratio (95% CI)	0.637 (0.511, 0.794)	
	Treatment P-value [a]	0.00002	
	Interaction P-value [b]	0.57505	
6 Months	Patients at Risk, Survival Est. (95% CI)	79, 0.46 (0.39, 0.53)	56, 0.32 (0.25, 0.39)
12 Months	Patients at Risk, Survival Est. (95% CI)	45, 0.26 (0.20, 0.33)	16, 0.10 (0.06, 0.15)
18 Months	Patients at Risk, Survival Est. (95% CI)	27, 0.17 (0.11, 0.22)	8, 0.06 (0.03, 0.11)
24 Months	Patients at Risk, Survival Est. (95% CI)	7, 0.12 (0.07, 0.18)	3, 0.04 (0.02, 0.08)
30 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.04 (0.02, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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=249)	Chemotherapy (N=239)
Overall	No. of Events (%)	199 (79.9)	198 (82.8)
	Median Survival Est. (Months) (95% CI)	5.65 (5.36, 6.57)	3.68 (3.35, 3.94)
	Hazard Ratio (95% CI)	0.633 (0.519, 0.772)	
	Treatment P-value [a]	<.00001	
	Interaction P-value [b]	0.28868	
6 Months	Patients at Risk, Survival Est. (95% CI)	104, 0.46 (0.39, 0.52)	61, 0.29 (0.23, 0.35)
12 Months	Patients at Risk, Survival Est. (95% CI)	61, 0.27 (0.21, 0.33)	19, 0.10 (0.07, 0.15)
18 Months	Patients at Risk, Survival Est. (95% CI)	36, 0.17 (0.12, 0.22)	14, 0.08 (0.04, 0.12)
24 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.13 (0.08, 0.18)	7, 0.06 (0.03, 0.10)
30 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.13 (0.08, 0.18)	1, 0.06 (0.03, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	39 (75.0)	58 (85.3)
	Median Survival Est. (Months) (95% CI)	5.42 (3.71, 7.33)	4.14 (3.52, 5.62)
	Hazard Ratio (95% CI)	0.809 (0.539, 1.214)	
	Treatment P-value [a]	0.29612	
	Interaction P-value [b]	0.28868	
6 Months	Patients at Risk, Survival Est. (95% CI)	18, 0.42 (0.27, 0.56)	20, 0.35 (0.23, 0.46)
12 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.14 (0.06, 0.26)	5, 0.10 (0.04, 0.19)
18 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.11 (0.04, 0.23)	1, 0.05 (0.01, 0.14)
24 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.11 (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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	183 (76.9)	197 (84.9)
	Median Survival Est. (Months) (95% CI)	5.65 (5.32, 7.20)	3.71 (3.52, 3.98)
	Hazard Ratio (95% CI)	0.594 (0.485, 0.729)	
	Treatment P-value [a]	<.00001	
	Interaction P-value [b]	0.03606	
6 Months	Patients at Risk, Survival Est. (95% CI)	101, 0.47 (0.41, 0.54)	56, 0.27 (0.22, 0.34)
12 Months	Patients at Risk, Survival Est. (95% CI)	58, 0.27 (0.21, 0.33)	14, 0.09 (0.05, 0.13)
18 Months	Patients at Risk, Survival Est. (95% CI)	34, 0.18 (0.13, 0.23)	10, 0.06 (0.03, 0.10)
24 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.14 (0.09, 0.19)	4, 0.04 (0.02, 0.08)
30 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.14 (0.09, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	55 (87.3)	59 (78.7)
	Median Survival Est. (Months) (95% CI)	5.39 (3.75, 5.78)	3.94 (3.02, 7.23)
	Hazard Ratio (95% CI)	0.932 (0.645, 1.346)	
	Treatment P-value [a]	0.68483	
	Interaction P-value [b]	0.03606	
6 Months	Patients at Risk, Survival Est. (95% CI)	21, 0.37 (0.25, 0.49)	25, 0.40 (0.28, 0.51)
12 Months	Patients at Risk, Survival Est. (95% CI)	9, 0.16 (0.08, 0.26)	10, 0.16 (0.08, 0.26)
18 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.10 (0.04, 0.20)	5, 0.11 (0.04, 0.20)
24 Months	Patients at Risk, Survival Est. (95% CI)	0	3, 0.08 (0.03, 0.18)
30 Months	Patients at Risk, Survival Est. (95% CI)	0	1, 0.08 (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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	104 (82.5)	107 (82.9)
	Median Survival Est. (Months) (95% CI)	5.55 (3.91, 7.16)	3.81 (3.35, 5.32)
	Hazard Ratio (95% CI)	0.740 (0.565, 0.970)	
	Treatment P-value [a]	0.03089	
	Interaction P-value [b]	0.53643	
6 Months	Patients at Risk, Survival Est. (95% CI)	53, 0.45 (0.36, 0.54)	35, 0.30 (0.22, 0.38)
12 Months	Patients at Risk, Survival Est. (95% CI)	27, 0.23 (0.16, 0.31)	16, 0.15 (0.09, 0.22)
18 Months	Patients at Risk, Survival Est. (95% CI)	16, 0.14 (0.09, 0.21)	10, 0.11 (0.06, 0.18)
24 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.12 (0.07, 0.19)	5, 0.08 (0.03, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	33 (76.7)	35 (79.5)
	Median Survival Est. (Months) (95% CI)	5.65 (3.45, 7.46)	3.35 (2.07, 5.62)
	Hazard Ratio (95% CI)	0.627 (0.389, 1.009)	
	Treatment P-value [a]	0.05419	
	Interaction P-value [b]	0.53643	
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)	9, 0.24 (0.12, 0.38)	2, 0.06 (0.01, 0.17)
18 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.15 (0.05, 0.28)	1, 0.03 (0.00, 0.13)
24 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.10 (0.02, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	101 (76.5)	114 (85.1)
	Median Survival Est. (Months) (95% CI)	5.55 (5.32, 7.20)	3.78 (3.52, 5.39)
	Hazard Ratio (95% CI)	0.598 (0.457, 0.784)	
	Treatment P-value [a]	0.00012	
	Interaction P-value [b]	0.53643	
6 Months	Patients at Risk, Survival Est. (95% CI)	52, 0.45 (0.36, 0.54)	35, 0.30 (0.22, 0.39)
12 Months	Patients at Risk, Survival Est. (95% CI)	31, 0.27 (0.19, 0.35)	6, 0.07 (0.03, 0.13)
18 Months	Patients at Risk, Survival Est. (95% CI)	20, 0.19 (0.12, 0.26)	4, 0.04 (0.01, 0.10)
24 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.14 (0.08, 0.22)	2, 0.03 (0.01, 0.08)
30 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.14 (0.08, 0.22)	1, 0.03 (0.01, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	87 (72.5)	101 (81.5)
	Median Survival Est. (Months) (95% CI)	7.23 (5.55, 8.41)	5.39 (3.71, 5.65)
	Hazard Ratio (95% CI)	0.631 (0.474, 0.842)	
	Treatment P-value [a]	0.00132	
	Interaction P-value [b]	0.75418	
6 Months	Patients at Risk, Survival Est. (95% CI)	58, 0.53 (0.43, 0.62)	40, 0.37 (0.28, 0.46)
12 Months	Patients at Risk, Survival Est. (95% CI)	35, 0.32 (0.23, 0.41)	14, 0.13 (0.08, 0.21)
18 Months	Patients at Risk, Survival Est. (95% CI)	24, 0.25 (0.17, 0.34)	9, 0.09 (0.04, 0.15)
24 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.20 (0.13, 0.29)	6, 0.08 (0.04, 0.14)
30 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.20 (0.13, 0.29)	1, 0.08 (0.04, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	151 (83.4)	155 (84.7)
	Median Survival Est. (Months) (95% CI)	5.39 (3.94, 5.65)	3.35 (2.30, 3.84)
	Hazard Ratio (95% CI)	0.669 (0.534, 0.839)	
	Treatment P-value [a]	0.00073	
	Interaction P-value [b]	0.75418	
6 Months	Patients at Risk, Survival Est. (95% CI)	64, 0.40 (0.32, 0.47)	41, 0.26 (0.20, 0.33)
12 Months	Patients at Risk, Survival Est. (95% CI)	32, 0.20 (0.14, 0.26)	10, 0.08 (0.05, 0.14)
18 Months	Patients at Risk, Survival Est. (95% CI)	16, 0.10 (0.06, 0.16)	6, 0.06 (0.03, 0.11)
24 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.07 (0.03, 0.13)	1, 0.03 (0.01, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	82 (88.2)	83 (87.4)
	Median Survival Est. (Months) (95% CI)	4.44 (3.71, 5.55)	3.02 (2.07, 3.55)
	Hazard Ratio (95% CI)	0.620 (0.456, 0.843)	
	Treatment P-value [a]	0.00238	
	Interaction P-value [b]	0.73705	
6 Months	Patients at Risk, Survival Est. (95% CI)	30, 0.36 (0.26, 0.46)	14, 0.16 (0.09, 0.25)
12 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.15 (0.09, 0.24)	4, 0.05 (0.02, 0.11)
18 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.06 (0.02, 0.13)	2, 0.04 (0.01, 0.10)
24 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.04 (0.01, 0.10)	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: No

Time Point	Statistics	Enfortumab Vedotin (N=208)	Chemotherapy (N=212)
Overall	No. of Events (%)	156 (75.0)	173 (81.6)
	Median Survival Est. (Months) (95% CI)	5.78 (5.52, 7.26)	4.40 (3.75, 5.55)
	Hazard Ratio (95% CI)	0.661 (0.532, 0.822)	
	Treatment P-value [a]	0.00019	
	Interaction P-value [b]	0.73705	
6 Months	Patients at Risk, Survival Est. (95% CI)	92, 0.49 (0.42, 0.56)	67, 0.37 (0.30, 0.43)
12 Months	Patients at Risk, Survival Est. (95% CI)	54, 0.29 (0.23, 0.36)	20, 0.13 (0.08, 0.18)
18 Months	Patients at Risk, Survival Est. (95% CI)	35, 0.20 (0.15, 0.27)	13, 0.09 (0.05, 0.14)
24 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.16 (0.11, 0.22)	6, 0.07 (0.04, 0.11)
30 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.16 (0.11, 0.22)	1, 0.07 (0.04, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	115 (81.6)	98 (87.5)
	Median Survival Est. (Months) (95% CI)	5.55 (4.44, 7.20)	3.65 (3.35, 5.13)
	Hazard Ratio (95% CI)	0.652 (0.498, 0.855)	
	Treatment P-value [a]	0.00137	
	Interaction P-value [b]	0.34278	
6 Months	Patients at Risk, Survival Est. (95% CI)	57, 0.46 (0.37, 0.54)	29, 0.29 (0.20, 0.38)
12 Months	Patients at Risk, Survival Est. (95% CI)	30, 0.24 (0.17, 0.32)	9, 0.10 (0.05, 0.16)
18 Months	Patients at Risk, Survival Est. (95% CI)	16, 0.14 (0.08, 0.21)	6, 0.06 (0.03, 0.12)
24 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.10 (0.05, 0.16)	2, 0.04 (0.01, 0.10)
30 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.10 (0.05, 0.16)	1, 0.04 (0.01, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	66 (75.9)	95 (81.2)
	Median Survival Est. (Months) (95% CI)	5.68 (3.94, 7.46)	3.52 (2.23, 3.94)
	Hazard Ratio (95% CI)	0.562 (0.409, 0.771)	
	Treatment P-value [a]	0.00051	
	Interaction P-value [b]	0.34278	
6 Months	Patients at Risk, Survival Est. (95% CI)	37, 0.48 (0.37, 0.59)	28, 0.30 (0.21, 0.39)
12 Months	Patients at Risk, Survival Est. (95% CI)	21, 0.27 (0.18, 0.38)	5, 0.07 (0.03, 0.13)
18 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.19 (0.11, 0.29)	3, 0.04 (0.01, 0.10)
24 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.12 (0.05, 0.22)	2, 0.04 (0.01, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	57 (78.1)	63 (80.8)
	Median Survival Est. (Months) (95% CI)	5.55 (4.60, 6.77)	4.17 (3.71, 5.62)
	Hazard Ratio (95% CI)	0.803 (0.561, 1.149)	
	Treatment P-value [a]	0.22584	
	Interaction P-value [b]	0.34278	
6 Months	Patients at Risk, Survival Est. (95% CI)	28, 0.41 (0.29, 0.52)	24, 0.34 (0.23, 0.45)
12 Months	Patients at Risk, Survival Est. (95% CI)	16, 0.23 (0.14, 0.34)	10, 0.16 (0.09, 0.26)
18 Months	Patients at Risk, Survival Est. (95% CI)	11, 0.17 (0.09, 0.27)	6, 0.12 (0.06, 0.22)
24 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.17 (0.09, 0.27)	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	77 (78.6)	83 (77.6)
	Median Survival Est. (Months) (95% CI)	5.65 (5.32, 7.52)	3.84 (3.02, 5.39)
	Hazard Ratio (95% CI)	0.717 (0.525, 0.978)	
	Treatment P-value [a]	0.04311	
	Interaction P-value [b]	0.49312	
6 Months	Patients at Risk, Survival Est. (95% CI)	45, 0.49 (0.39, 0.59)	32, 0.35 (0.26, 0.45)
12 Months	Patients at Risk, Survival Est. (95% CI)	26, 0.28 (0.20, 0.38)	14, 0.18 (0.10, 0.26)
18 Months	Patients at Risk, Survival Est. (95% CI)	17, 0.20 (0.13, 0.29)	9, 0.12 (0.06, 0.20)
24 Months	Patients at Risk, Survival Est. (95% CI)	4, 0.15 (0.08, 0.23)	5, 0.10 (0.04, 0.17)
30 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.15 (0.08, 0.23)	1, 0.10 (0.04, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	161 (79.3)	173 (86.5)
	Median Survival Est. (Months) (95% CI)	5.55 (4.44, 6.08)	3.71 (3.45, 4.14)
	Hazard Ratio (95% CI)	0.628 (0.506, 0.780)	
	Treatment P-value [a]	0.00001	
	Interaction P-value [b]	0.49312	
6 Months	Patients at Risk, Survival Est. (95% CI)	77, 0.43 (0.36, 0.50)	49, 0.28 (0.22, 0.35)
12 Months	Patients at Risk, Survival Est. (95% CI)	41, 0.23 (0.17, 0.29)	10, 0.06 (0.03, 0.11)
18 Months	Patients at Risk, Survival Est. (95% CI)	23, 0.14 (0.09, 0.20)	6, 0.05 (0.02, 0.09)
24 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.11 (0.06, 0.17)	2, 0.03 (0.01, 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	207 (79.0)	225 (83.3)
	Median Survival Est. (Months) (95% CI)	5.62 (5.32, 6.34)	3.78 (3.55, 4.17)
	Hazard Ratio (95% CI)	0.657 (0.543, 0.794)	
	Treatment P-value [a]	0.00002	
	Interaction P-value [b]	0.85448	
6 Months	Patients at Risk, Survival Est. (95% CI)	107, 0.45 (0.39, 0.51)	72, 0.30 (0.25, 0.36)
12 Months	Patients at Risk, Survival Est. (95% CI)	59, 0.25 (0.20, 0.30)	23, 0.11 (0.07, 0.15)
18 Months	Patients at Risk, Survival Est. (95% CI)	37, 0.17 (0.12, 0.22)	14, 0.08 (0.05, 0.12)
24 Months	Patients at Risk, Survival Est. (95% CI)	12, 0.13 (0.09, 0.18)	6, 0.05 (0.03, 0.09)
30 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.13 (0.09, 0.18)	1, 0.05 (0.03, 0.09)

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	31 (79.5)	31 (83.8)
	Median Survival Est. (Months) (95% CI)	5.55 (3.71, 7.46)	3.61 (2.10, 5.68)
	Hazard Ratio (95% CI)	0.690 (0.419, 1.137)	
	Treatment P-value [a]	0.11012	
	Interaction P-value [b]	0.85448	
6 Months	Patients at Risk, Survival Est. (95% CI)	15, 0.45 (0.28, 0.61)	9, 0.29 (0.15, 0.45)
12 Months	Patients at Risk, Survival Est. (95% CI)	8, 0.24 (0.11, 0.39)	1, 0.04 (0.00, 0.17)
18 Months	Patients at Risk, Survival Est. (95% CI)	3, 0.10 (0.03, 0.24)	1, 0.04 (0.00, 0.17)
24 Months	Patients at Risk, Survival Est. (95% CI)	0	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	43 (70.5)	42 (84.0)
	Median Survival Est. (Months) (95% CI)	7.59 (5.78, 11.10)	5.52 (3.65, 7.36)
	Hazard Ratio (95% CI)	0.506 (0.330, 0.776)	
	Treatment P-value [a]	0.00065	
	Interaction P-value [b]	0.16291	
6 Months	Patients at Risk, Survival Est. (95% CI)	34, 0.61 (0.47, 0.73)	16, 0.39 (0.25, 0.53)
12 Months	Patients at Risk, Survival Est. (95% CI)	20, 0.36 (0.24, 0.48)	3, 0.07 (0.02, 0.18)
18 Months	Patients at Risk, Survival Est. (95% CI)	13, 0.26 (0.15, 0.38)	1, 0.02 (0.00, 0.11)
24 Months	Patients at Risk, Survival Est. (95% CI)	5, 0.22 (0.12, 0.34)	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	167 (80.7)	178 (82.8)
	Median Survival Est. (Months) (95% CI)	5.45 (4.60, 5.65)	3.68 (3.38, 4.04)
	Hazard Ratio (95% CI)	0.711 (0.575, 0.878)	
	Treatment P-value [a]	0.00210	
	Interaction P-value [b]	0.16291	
6 Months	Patients at Risk, Survival Est. (95% CI)	76, 0.41 (0.34, 0.48)	54, 0.29 (0.23, 0.36)
12 Months	Patients at Risk, Survival Est. (95% CI)	40, 0.22 (0.16, 0.28)	19, 0.11 (0.07, 0.16)
18 Months	Patients at Risk, Survival Est. (95% CI)	22, 0.13 (0.09, 0.18)	12, 0.08 (0.05, 0.13)
24 Months	Patients at Risk, Survival Est. (95% CI)	6, 0.10 (0.06, 0.16)	4, 0.05 (0.03, 0.10)
30 Months	Patients at Risk, Survival Est. (95% CI)	1, 0.10 (0.06, 0.16)	1, 0.05 (0.03, 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.

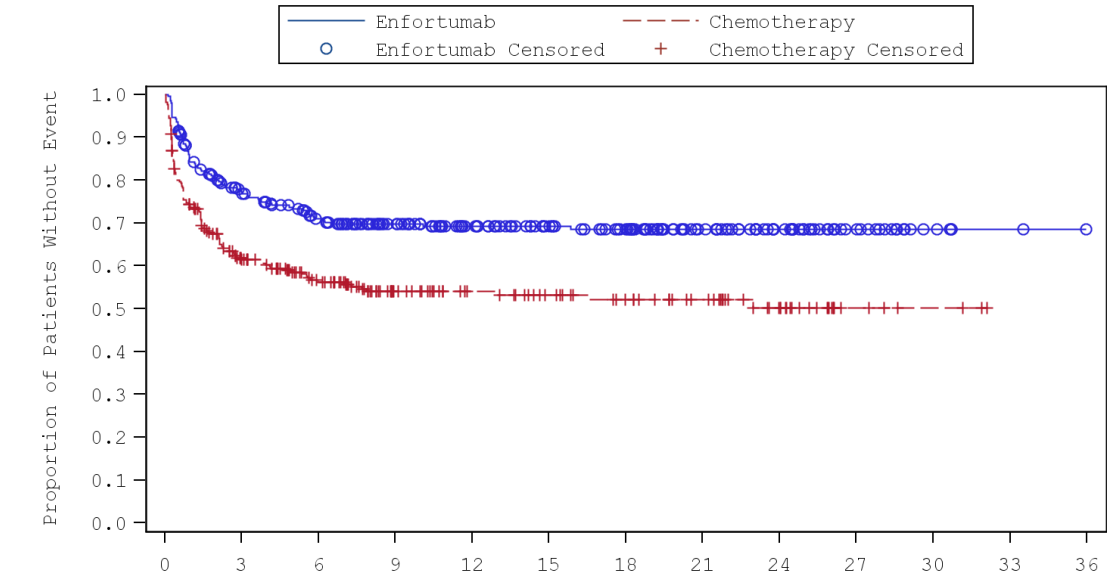
SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_MOR_KM.SAS
Date/time of run: 06DEC2021 14:50 Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

3 Sicherheit

3.1 Kaplan-Meier Kurven zu den SOC und PT der unerwünschten Ereignisse

3.1.1 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

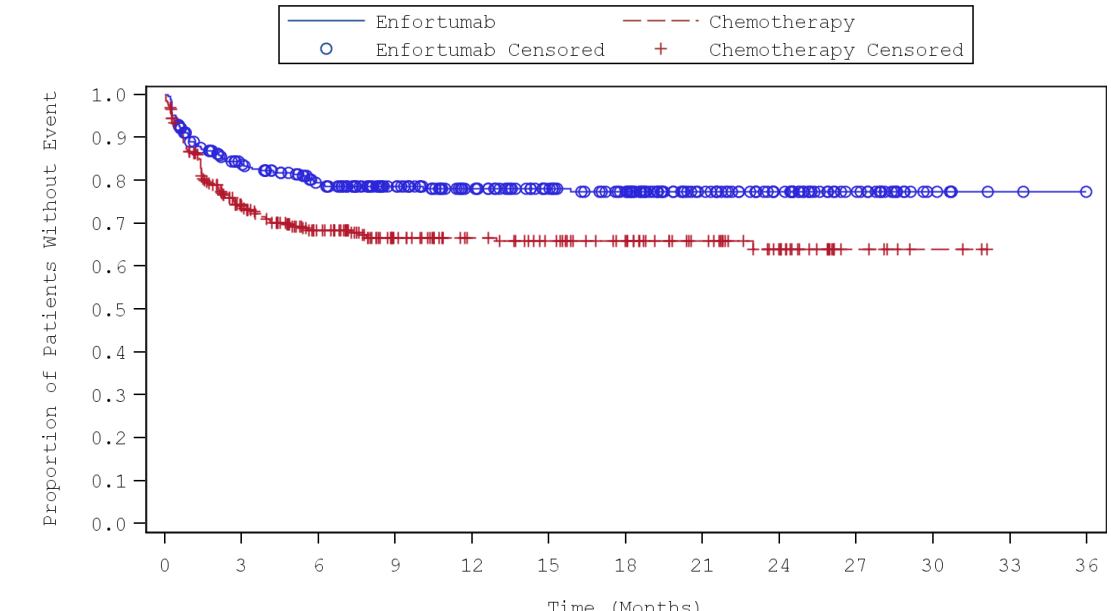
Enfortumab:	296	208	175	144	118	99	86	57	38	19	6	2	0
Chemotherapy:	291	154	118	79	64	55	46	37	23	6	3	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.563 (0.427, 0.741)
P-value: 0.00003

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

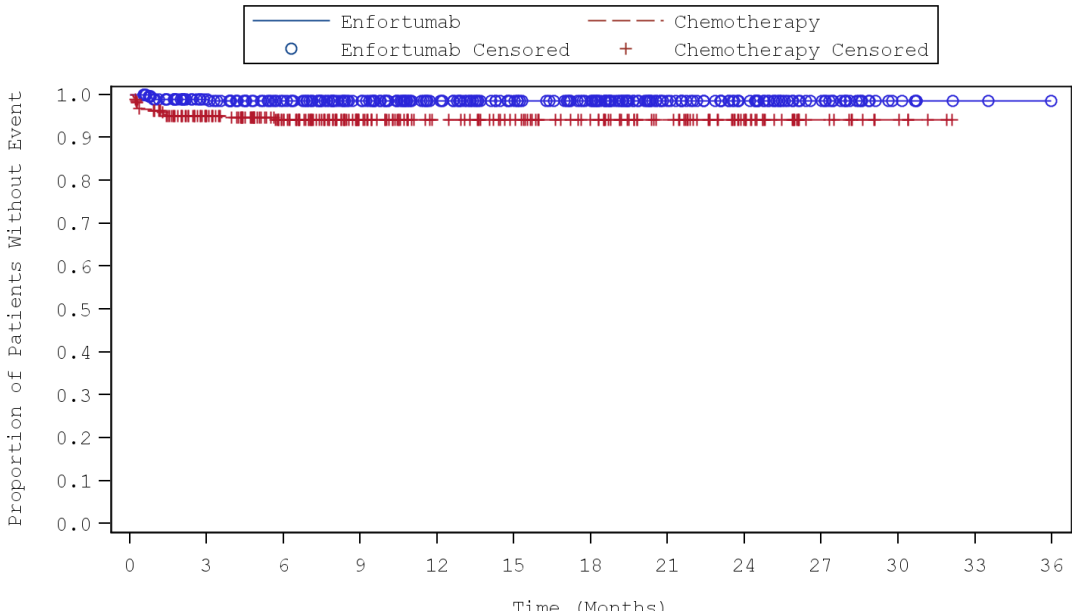
Enfortumab:	296	226	195	162	135	115	101	67	47	25	7	2	0
Chemotherapy:	291	184	139	99	80	70	58	43	28	8	3	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.606 (0.438, 0.839)
P-value: 0.00234

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

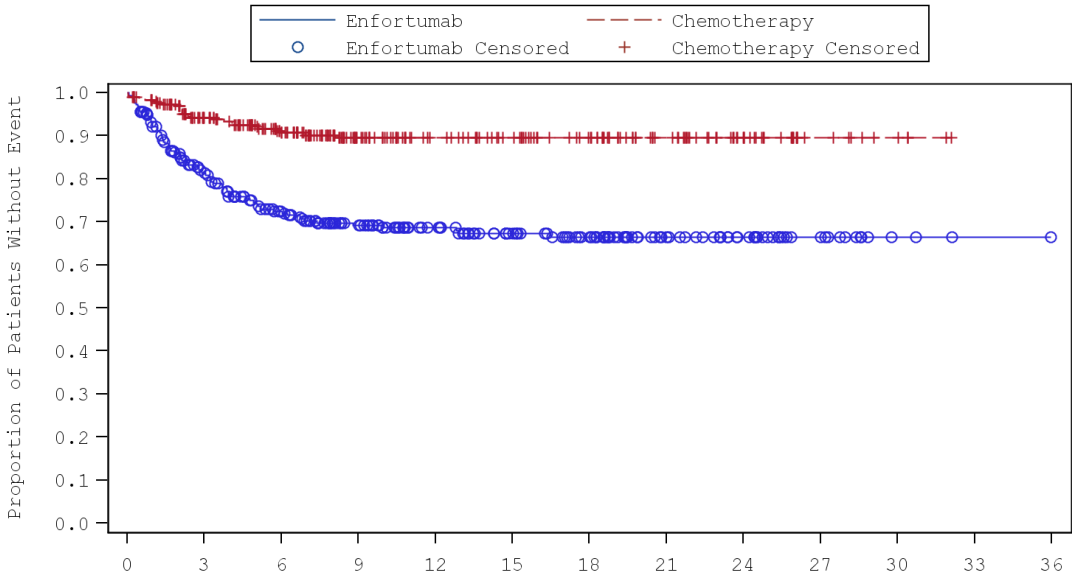
Enfortumab:	296	261	232	199	164	139	122	75	53	27	7	2	0
Chemotherapy:	291	236	195	139	111	97	81	61	38	14	6	0	0

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

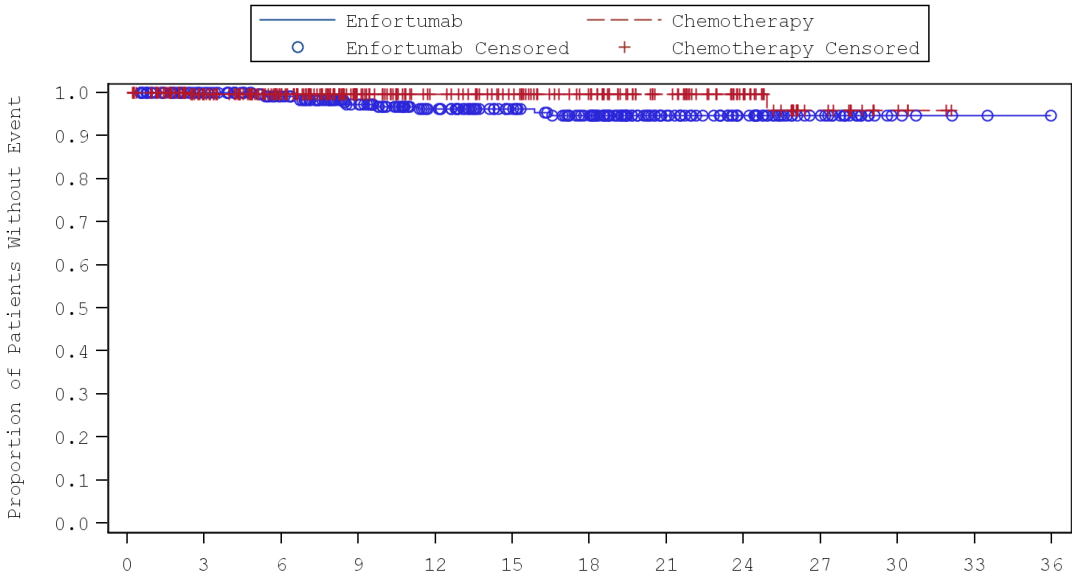
Enfortumab:	296	213	165	129	104	85	70	41	28	13	3	1	0
Chemotherapy:	291	233	186	129	102	88	72	49	29	10	5	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 3.671 (2.364, 5.701)
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: Cataract (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

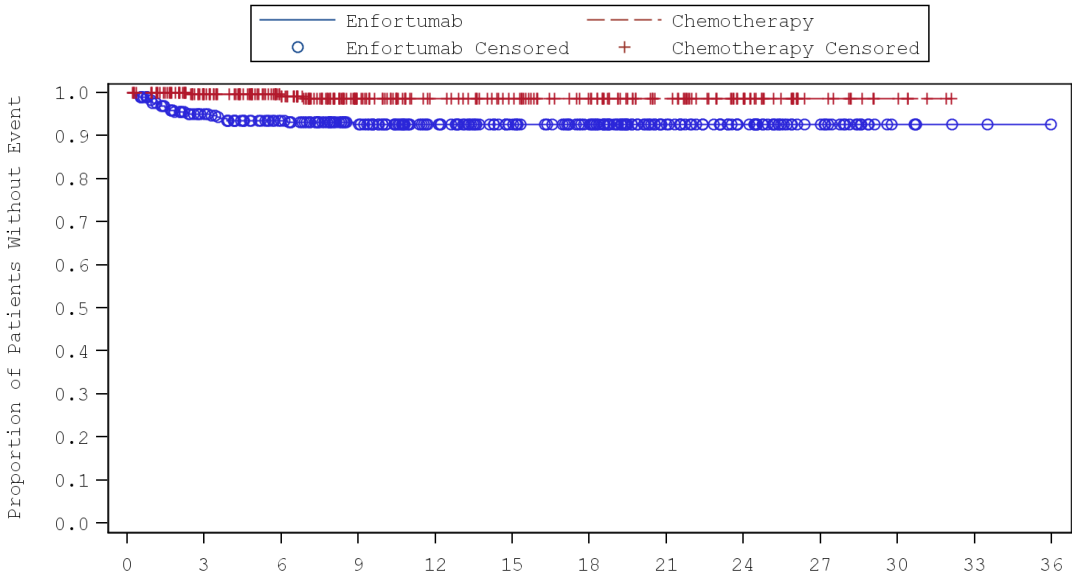
Enfortumab:	296	263	232	193	158	133	114	69	48	24	5	2	0
Chemotherapy:	291	247	205	147	118	103	85	61	38	13	5	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 4.128 (0.895, 19.039)
P-value: 0.04907

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

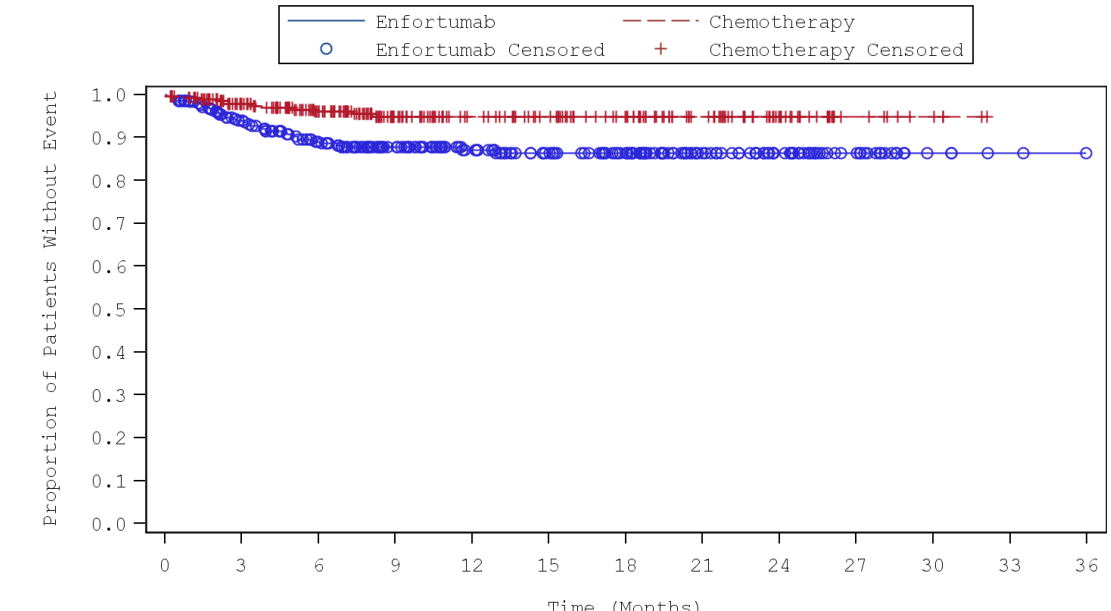
Enfortumab:	296	251	219	184	152	128	111	68	47	24	6	2	0
Chemotherapy:	291	247	204	145	116	101	84	60	38	14	6	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 6.405 (1.902, 21.571)
P-value: 0.00057

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

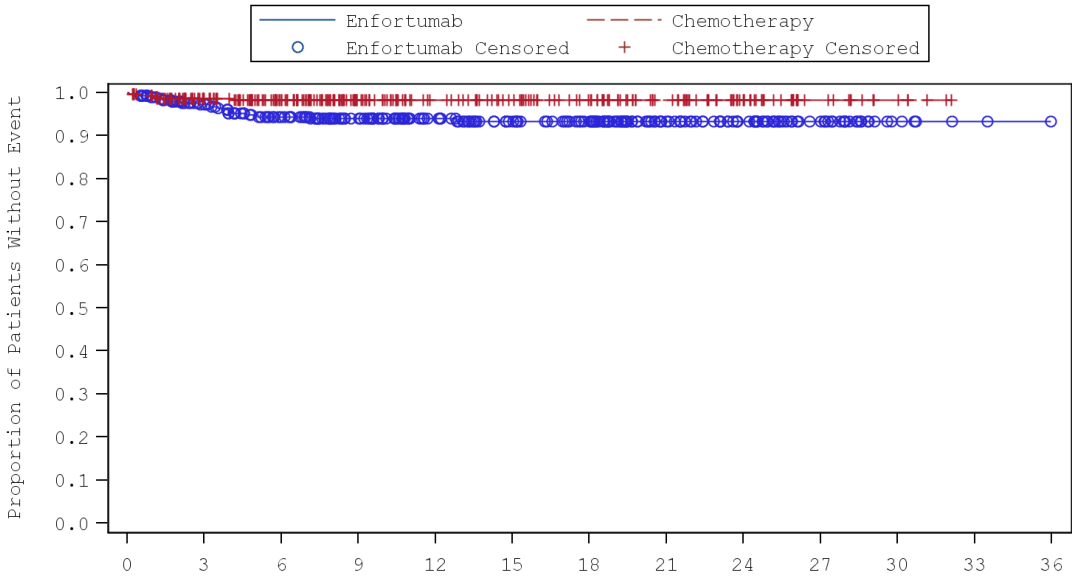
Enfortumab:	296	246	206	168	136	115	98	60	41	20	5	2	0
Chemotherapy:	291	242	196	137	110	96	79	55	32	10	5	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 2.721 (1.406, 5.266)
P-value: 0.00197

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

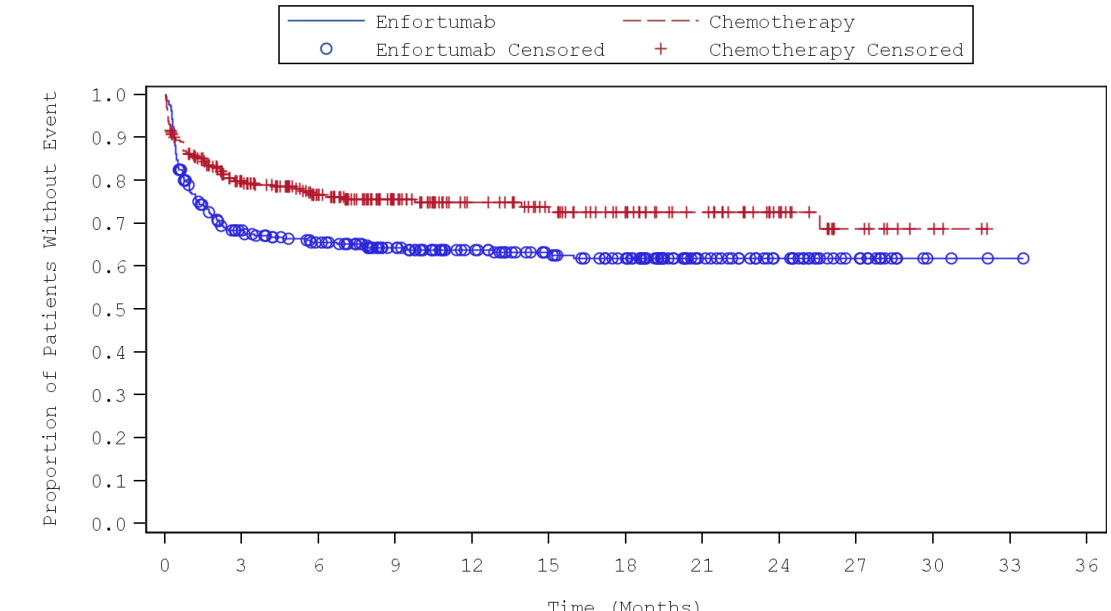
Enfortumab:	296	255	220	186	153	131	115	71	50	26	6	2	0
Chemotherapy:	291	244	204	146	117	102	84	60	37	14	6	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 3.386 (1.246, 9.202)
P-value: 0.01110

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

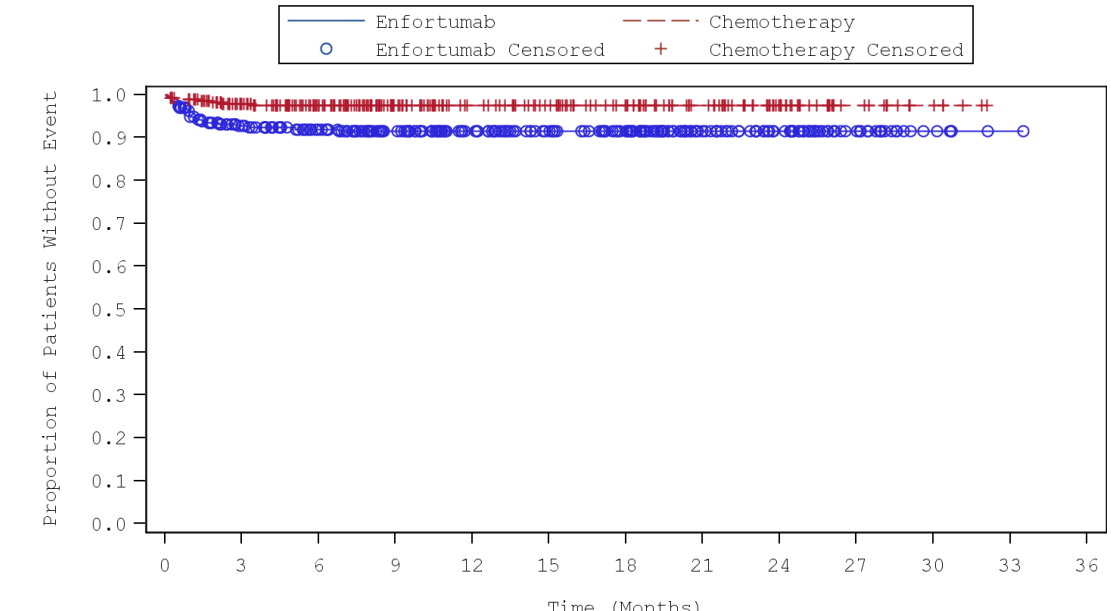
Enfortumab:	296	184	162	135	110	93	81	47	32	16	3	1	0
Chemotherapy:	291	196	153	105	79	65	51	39	24	10	4	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 1.566 (1.156, 2.121)
P-value: 0.00364

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

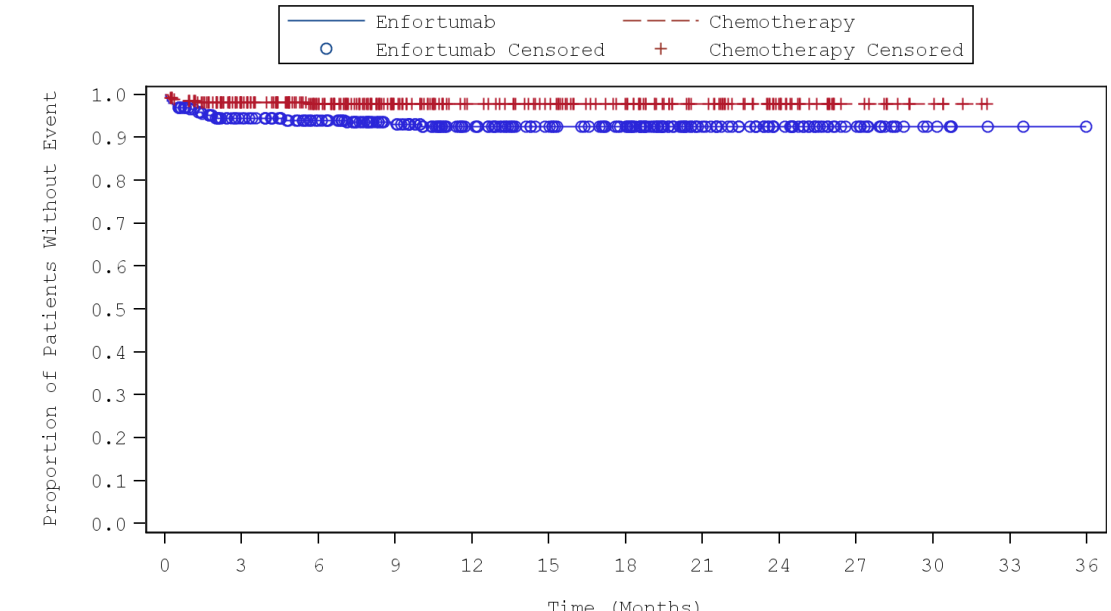
Enfortumab:	296	243	214	182	151	128	111	68	47	22	6	1	0
Chemotherapy:	291	243	202	145	116	101	83	60	37	14	6	0	0

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

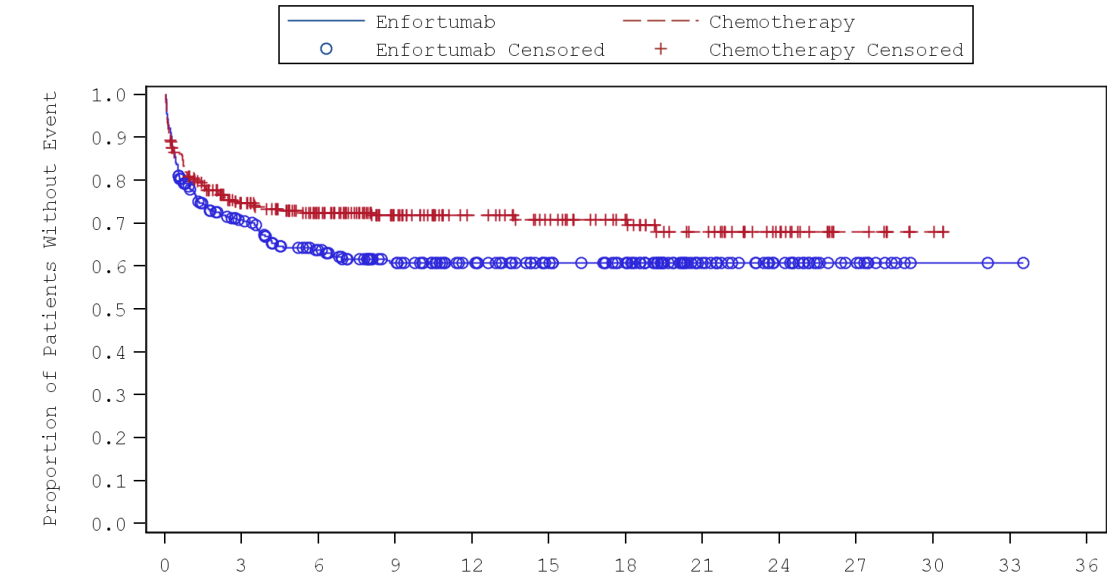
Enfortumab:	296	248	221	186	153	130	114	67	46	23	7	2	0
Chemotherapy:	291	244	202	144	115	101	83	59	36	14	6	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 3.117 (1.250, 7.771)
P-value: 0.01013

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

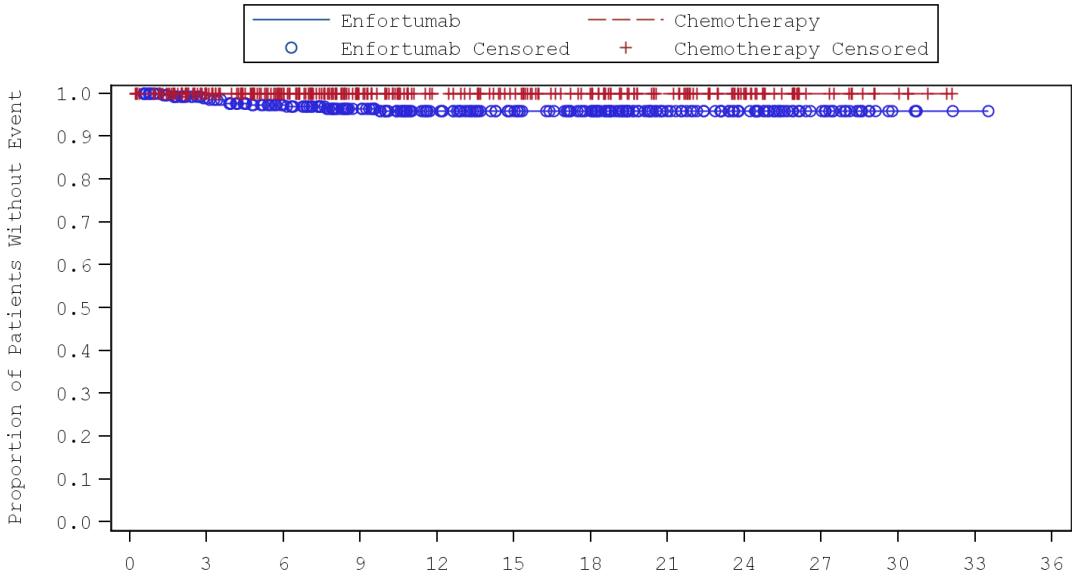
Enfortumab:	296	189	153	127	108	91	81	45	29	13	2	1	0
Chemotherapy:	291	183	147	102	79	67	54	38	24	9	3	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 1.341 (1.006, 1.789)
P-value: 0.04535

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: Gait disturbance (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

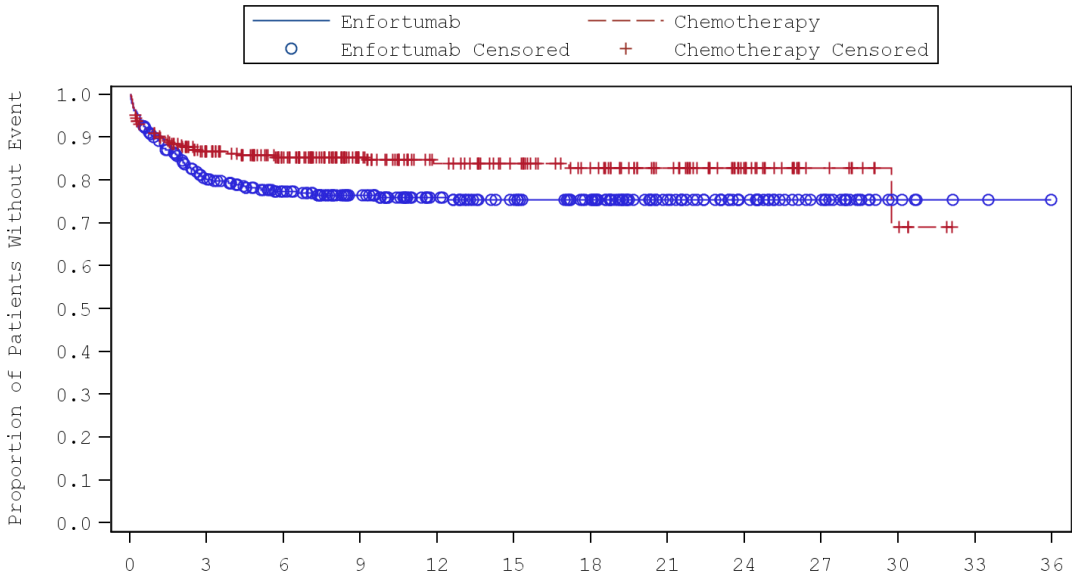
Enfortumab:	296	261	228	192	156	132	115	70	49	24	5	1	0
Chemotherapy:	291	248	206	148	119	104	86	62	38	14	6	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): NA (NA, NA)
P-value: 0.00435

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

Figure TEAE.KM.SAF: Time to First Treatment Emergent Adverse Event (Months) - General disorders and administration site conditions: Pyrexia (Safety Analysis Set) Subgroup: Overall, Level: NA



No. of Subjects at Risk

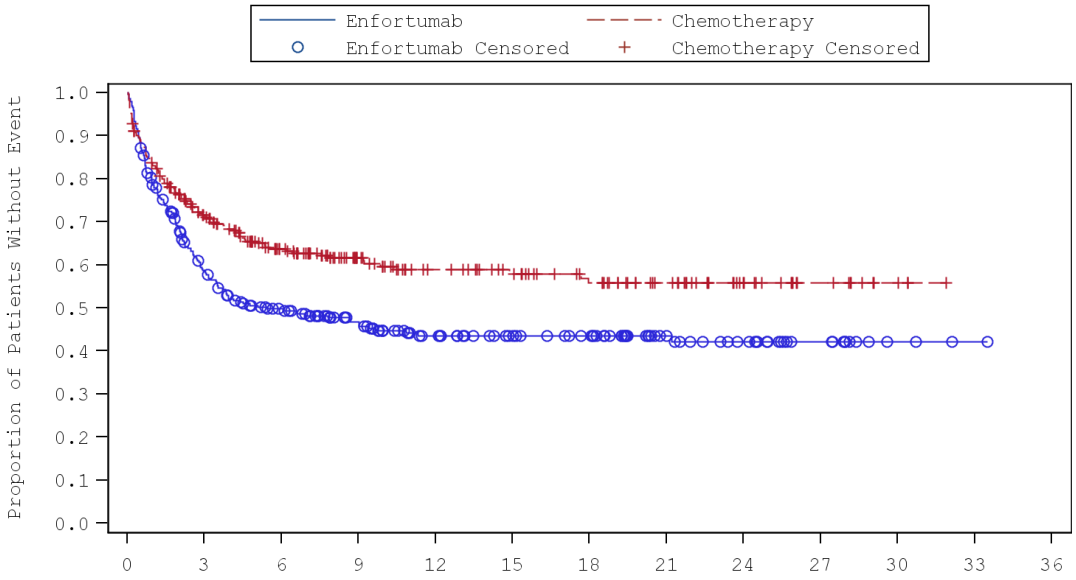
Enfortumab:	296	215	181	153	125	108	95	61	41	24	6	2	0
Chemotherapy:	291	219	182	130	103	89	74	55	33	13	5	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 1.472 (1.006, 2.153)
P-value: 0.04544

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (29.73, 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

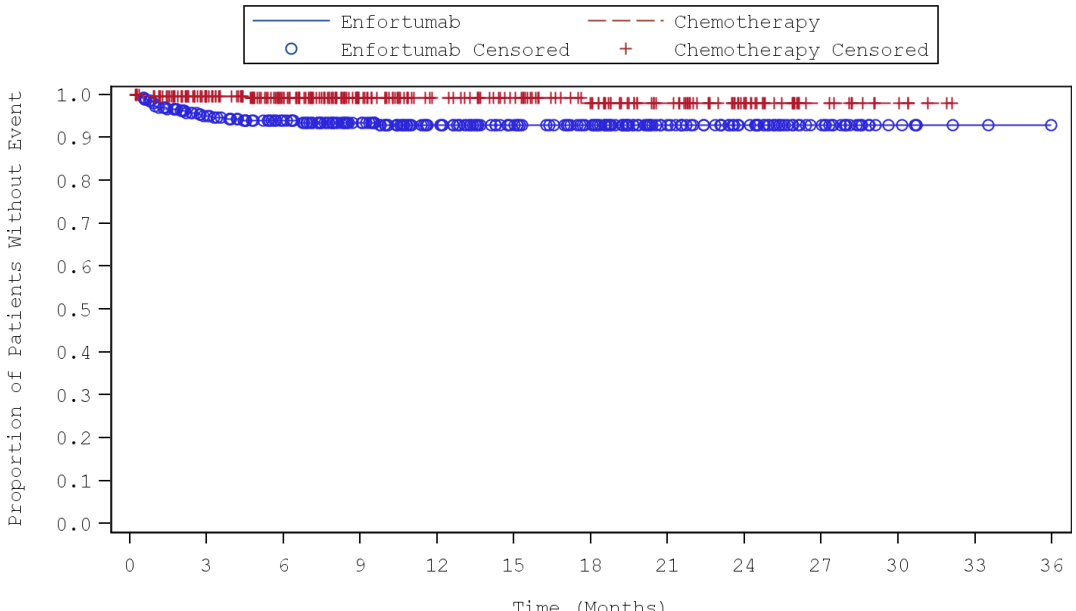
Enfortumab:	296	161	123	96	72	60	53	31	23	12	3	1	0
Chemotherapy:	291	185	135	94	73	63	51	37	21	11	4	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 1.451 (1.136, 1.853)
P-value: 0.00276

Enfortumab Median (95% CI): 5.45 (3.48, 11.33)
Chemotherapy Median (95% CI): NC (17.68, 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

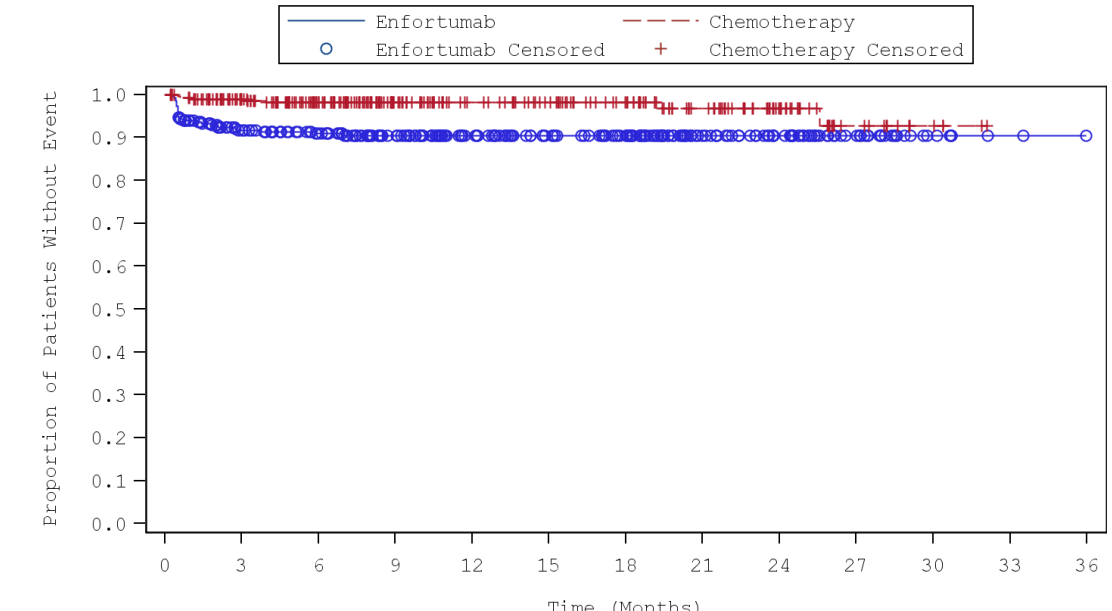
Enfortumab:	296	250	220	185	151	127	111	71	51	26	7	2	0
Chemotherapy:	291	247	205	147	119	104	85	61	38	14	6	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 6.569 (1.938, 22.272)
P-value: 0.00051

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

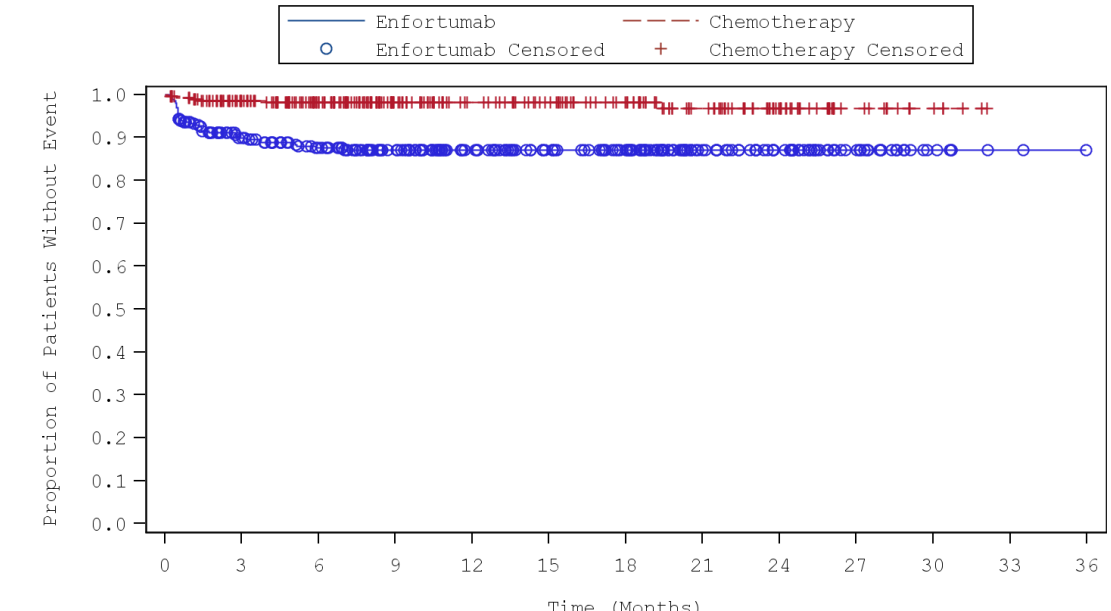
Enfortumab:	296	239	213	182	149	128	112	69	50	25	7	2	0
Chemotherapy:	291	246	203	145	117	103	85	60	37	13	5	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 3.766 (1.637, 8.666)
P-value: 0.00083

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

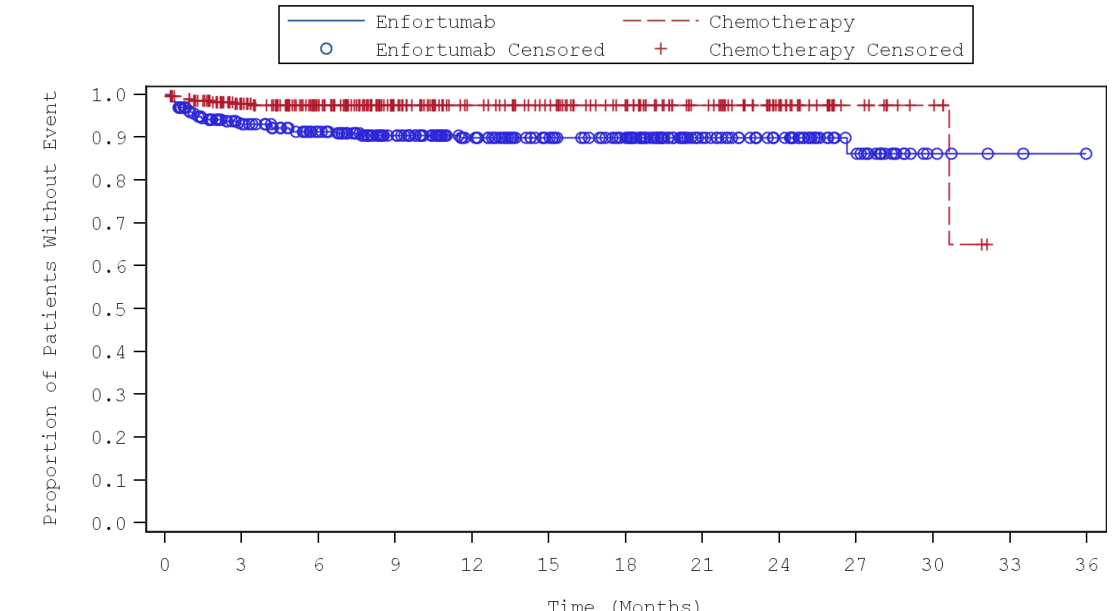
Enfortumab:	296	235	207	176	144	122	106	66	48	24	7	2	0
Chemotherapy:	291	247	205	147	119	104	86	61	38	14	6	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 6.021 (2.533, 14.313)
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

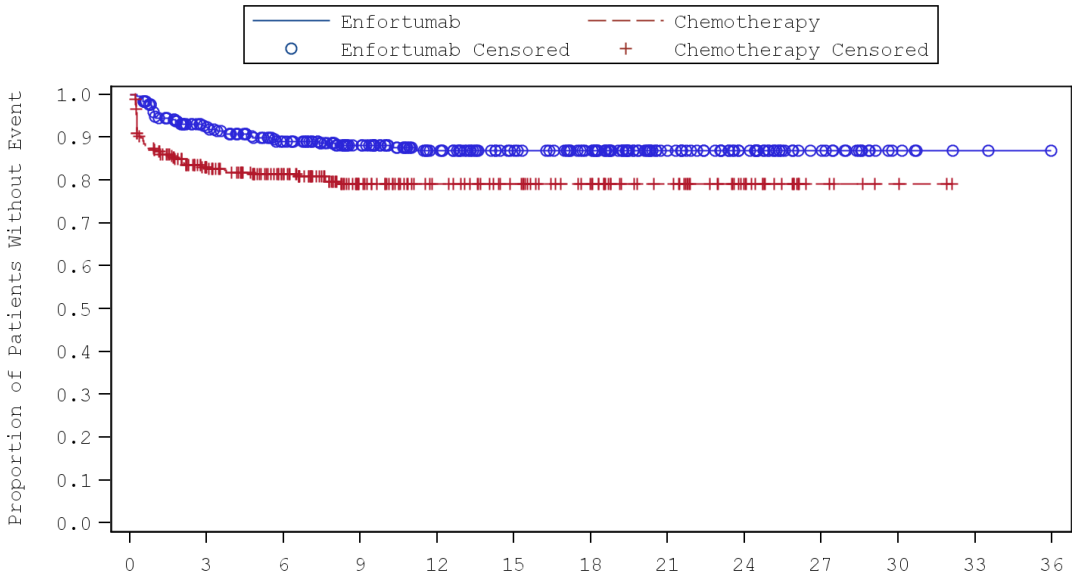
Enfortumab:	296	244	215	181	148	124	109	66	48	23	5	2	0
Chemotherapy:	291	245	202	145	116	102	84	60	37	13	6	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 4.118 (1.794, 9.454)
P-value: 0.00030

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): NC (30.62, 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

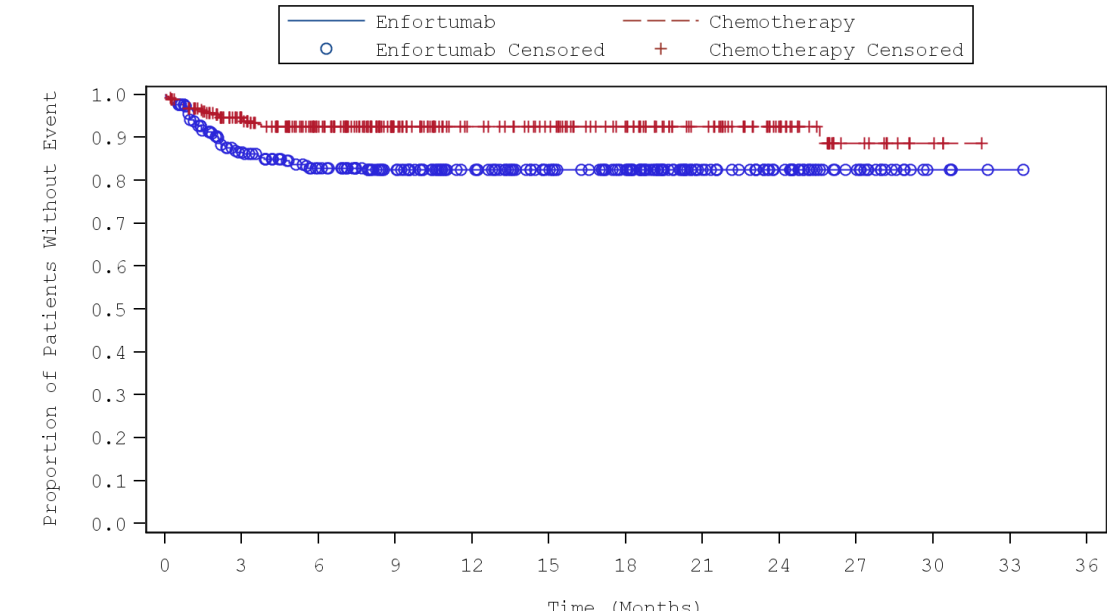
Enfortumab:	296	243	207	172	140	117	102	62	43	21	6	2	0
Chemotherapy:	291	202	164	111	87	74	60	44	26	7	3	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.493 (0.320, 0.759)
P-value: 0.00117

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

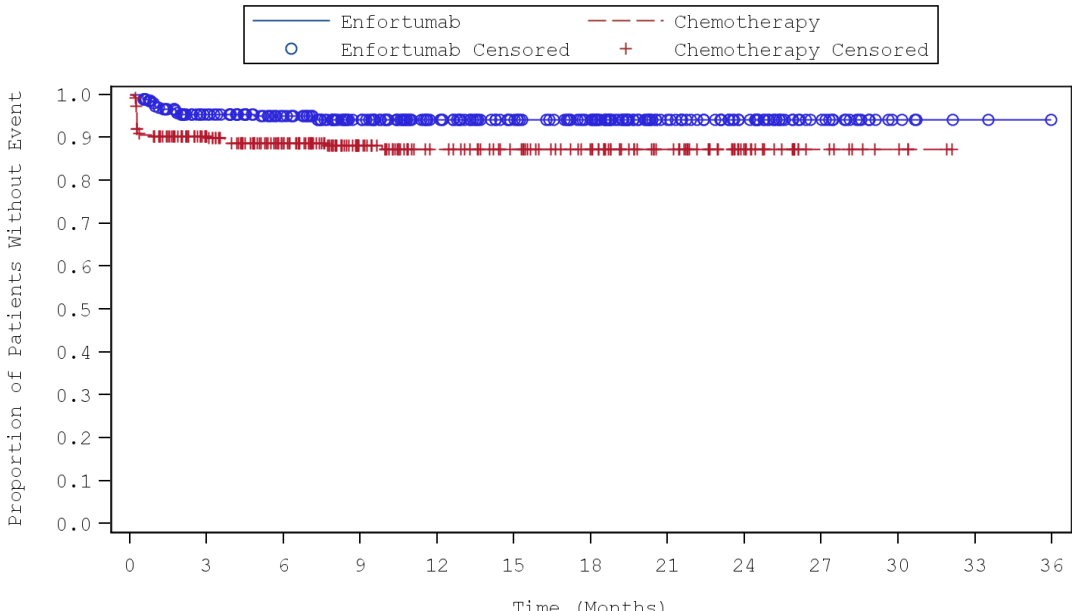
Enfortumab:	296	228	195	169	143	121	105	61	44	22	5	1	0
Chemotherapy:	291	236	191	137	109	97	79	57	35	12	4	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 2.261 (1.350, 3.786)
P-value: 0.00145

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

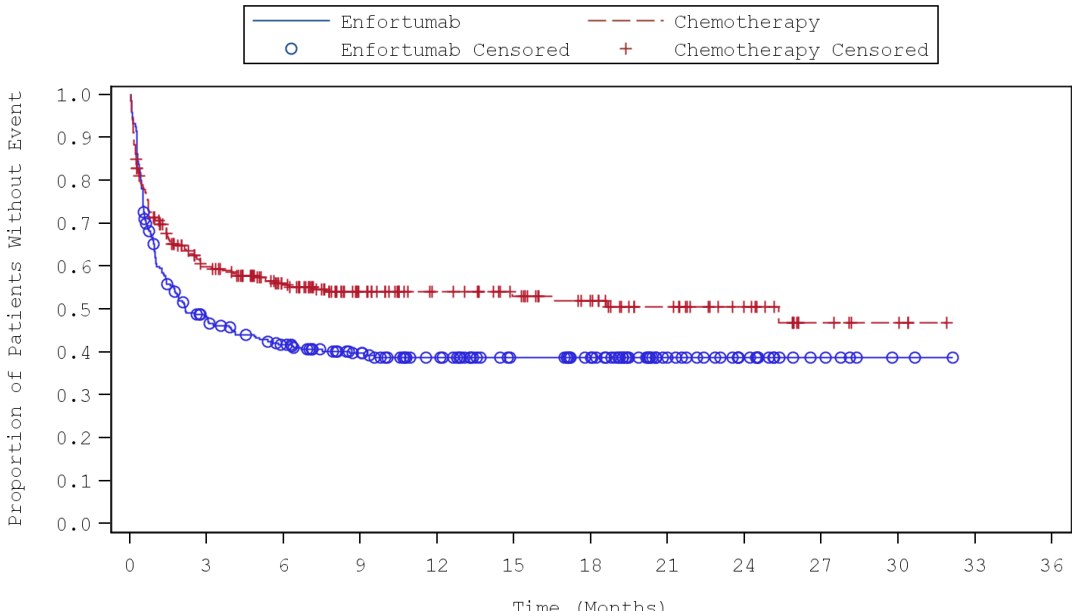
Enfortumab:	296	250	221	186	151	127	110	66	46	22	6	2	0
Chemotherapy:	291	222	181	128	101	88	73	51	29	11	5	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.406 (0.223, 0.739)
P-value: 0.00249

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

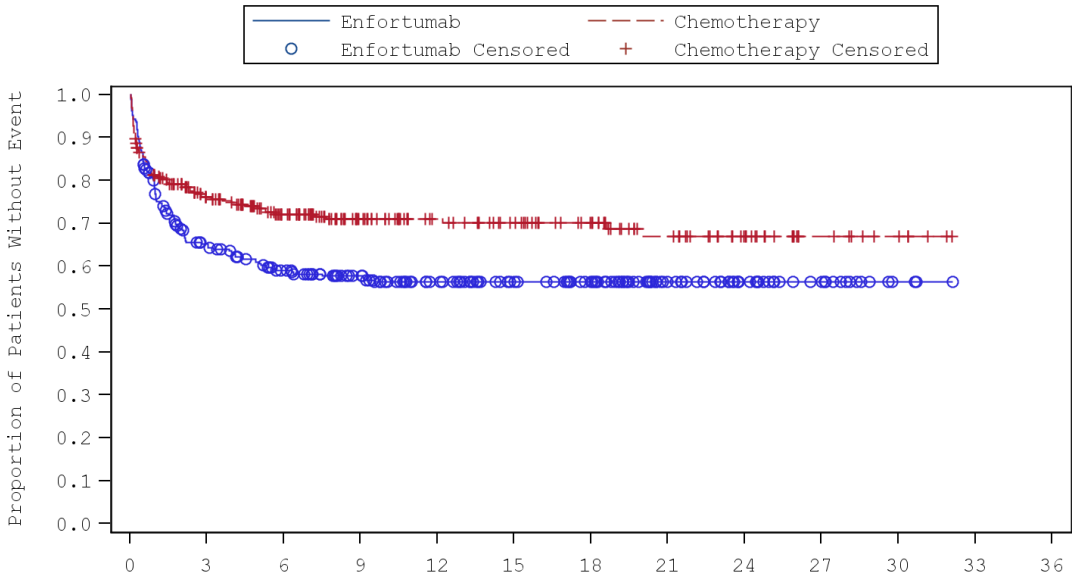
Enfortumab:	296	133	109	89	74	59	53	29	18	7	2	0	0
Chemotherapy:	291	155	119	80	63	53	42	30	19	7	4	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 1.400 (1.115, 1.758)
P-value: 0.00353

Enfortumab Median (95% CI): 2.17 (1.41, 4.11)
Chemotherapy Median (95% CI): 25.33 (5.68, 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

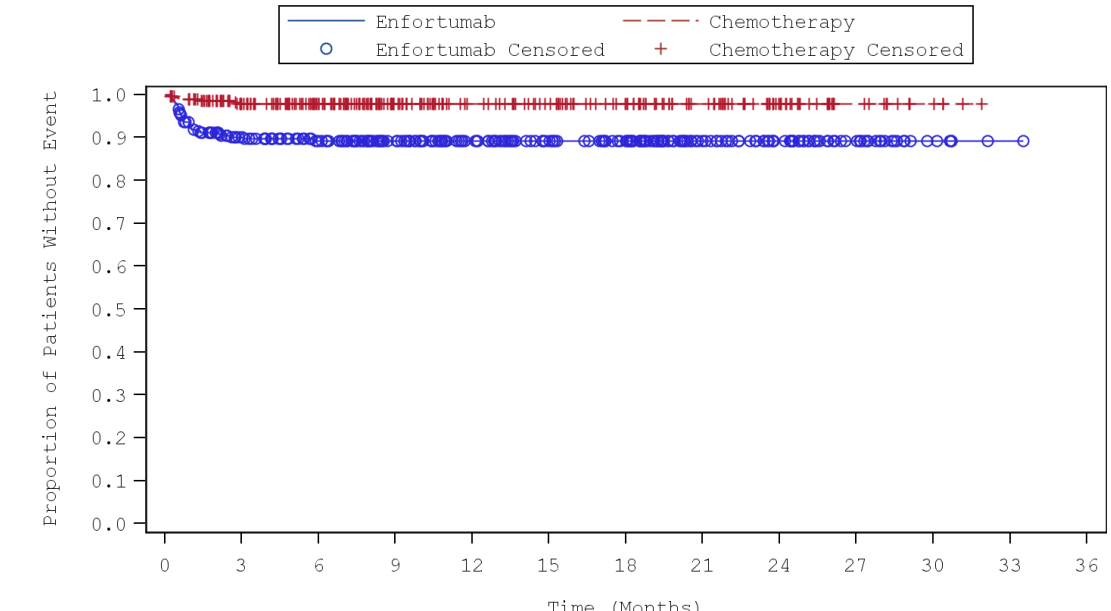
Enfortumab:	296	176	146	124	101	84	73	44	27	15	3	0	0
Chemotherapy:	291	189	148	105	82	70	56	39	25	11	6	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 1.480 (1.118, 1.960)
P-value: 0.00558

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

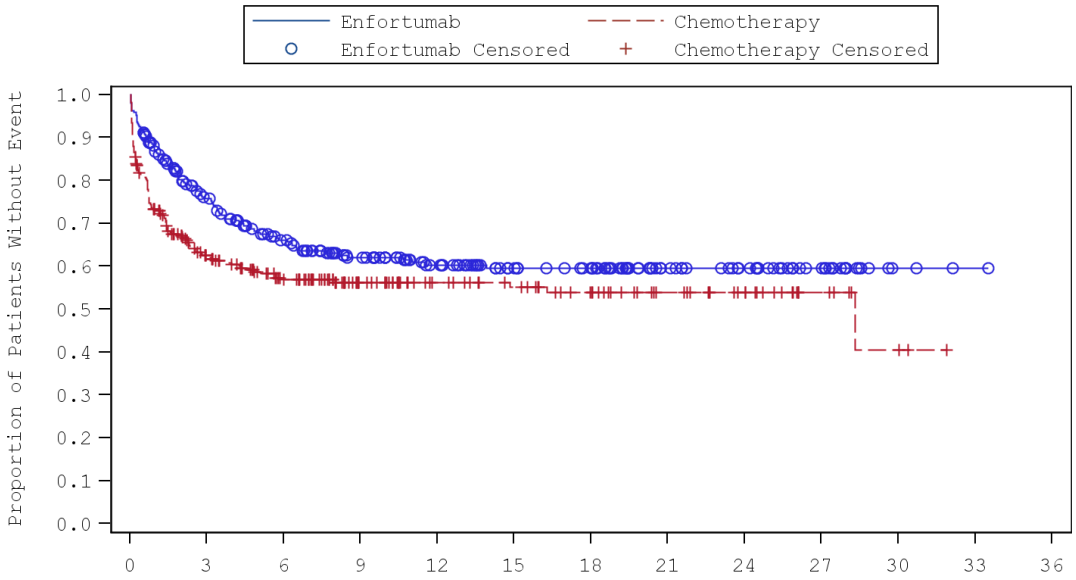
Enfortumab:	296	240	213	180	149	125	110	67	47	23	6	1	0
Chemotherapy:	291	244	203	145	116	101	83	59	36	13	5	0	0

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

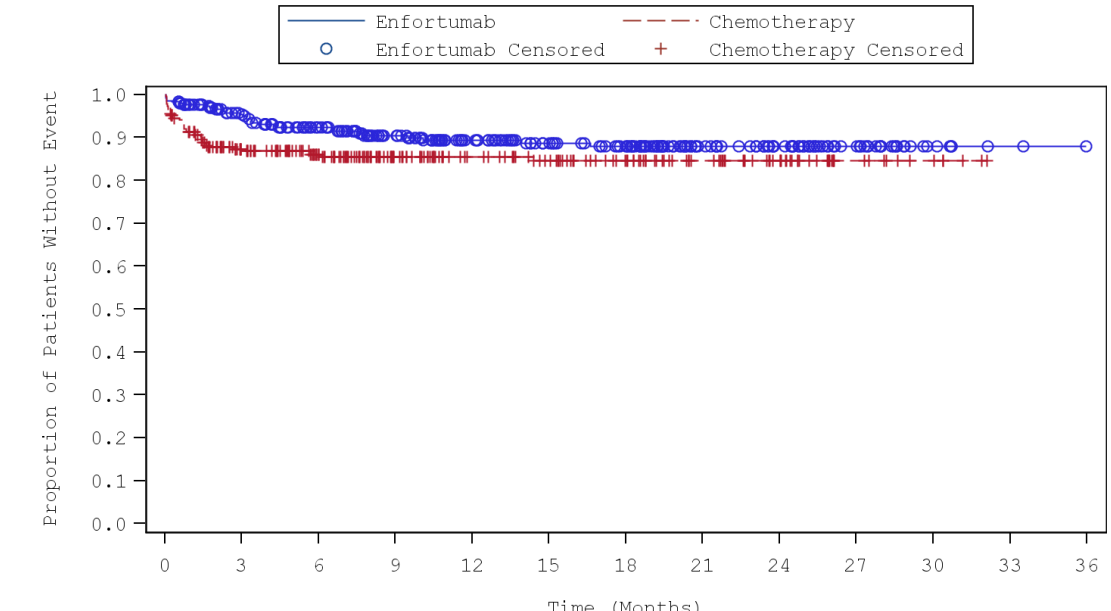
Enfortumab:	296	198	154	122	97	77	70	43	33	19	3	1	0
Chemotherapy:	291	155	119	79	59	51	41	29	21	8	3	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.710 (0.546, 0.924)
P-value: 0.01093

Enfortumab Median (95% CI): NC (NC, NC)
Chemotherapy Median (95% CI): 28.32 (14.85, 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

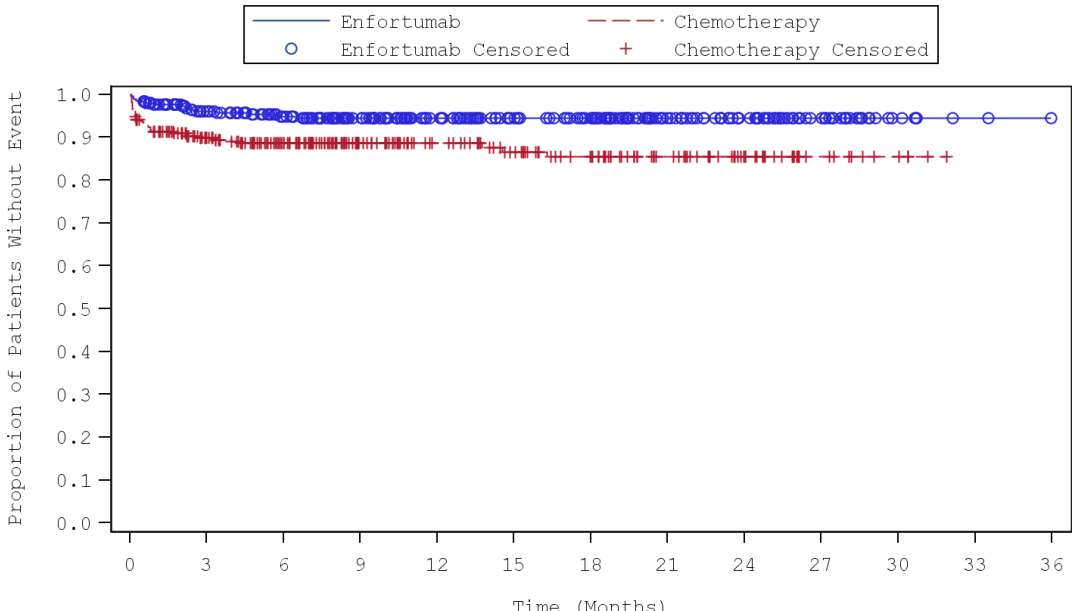
Enfortumab:	296	252	215	179	144	121	107	65	48	26	7	2	0
Chemotherapy:	291	215	175	124	98	85	68	49	34	12	6	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.608 (0.376, 0.983)
P-value: 0.04074

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

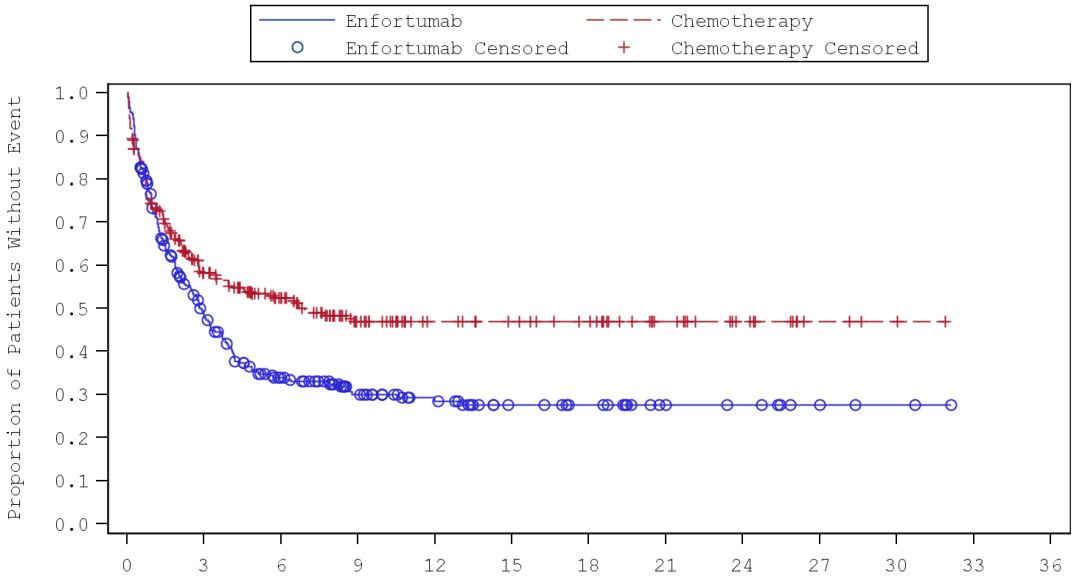
Enfortumab:	296	252	221	186	153	128	114	72	51	27	7	2	0
Chemotherapy:	291	223	183	127	101	85	70	48	31	11	5	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.400 (0.218, 0.733)
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) - Nervous system disorders (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

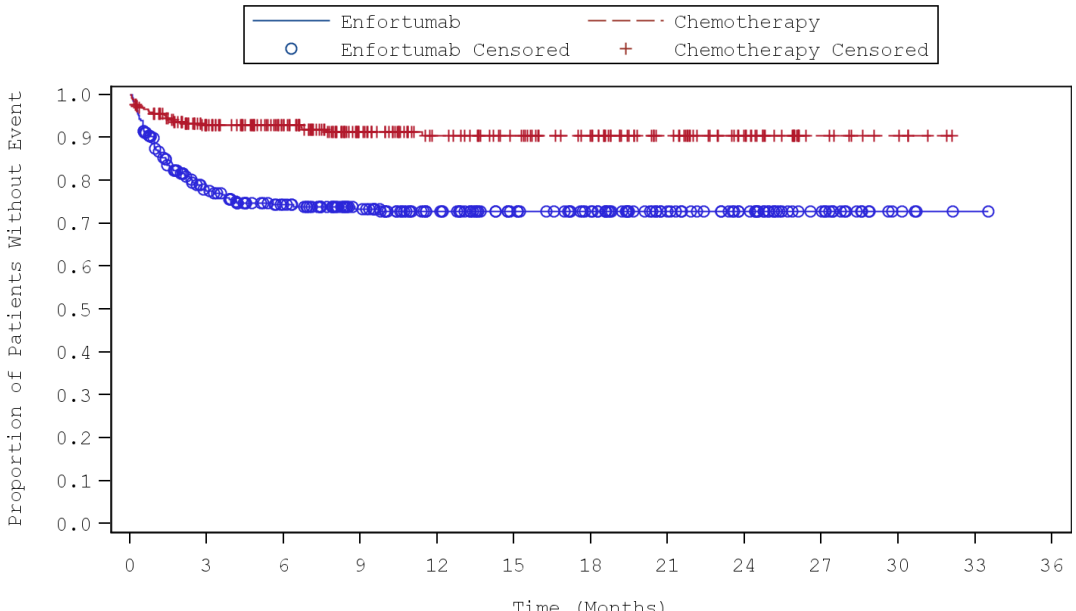
Enfortumab:	296	124	74	49	34	22	18	9	8	4	2	0	0
Chemotherapy:	291	139	99	62	43	38	33	20	12	4	2	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 1.426 (1.144, 1.778)
P-value: 0.00148

Enfortumab Median (95% CI): 2.83 (2.20, 3.68)
Chemotherapy Median (95% CI): 6.93 (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

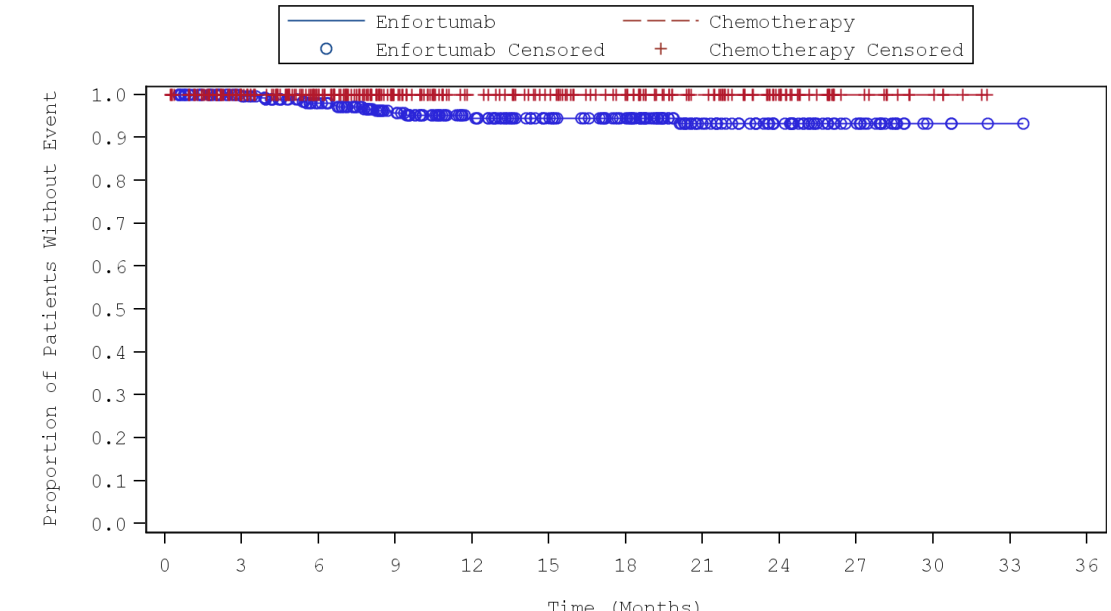
Enfortumab:	296	201	168	138	111	91	79	54	40	21	5	1	0
Chemotherapy:	291	229	191	135	106	92	78	55	35	12	6	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 3.281 (2.067, 5.207)
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

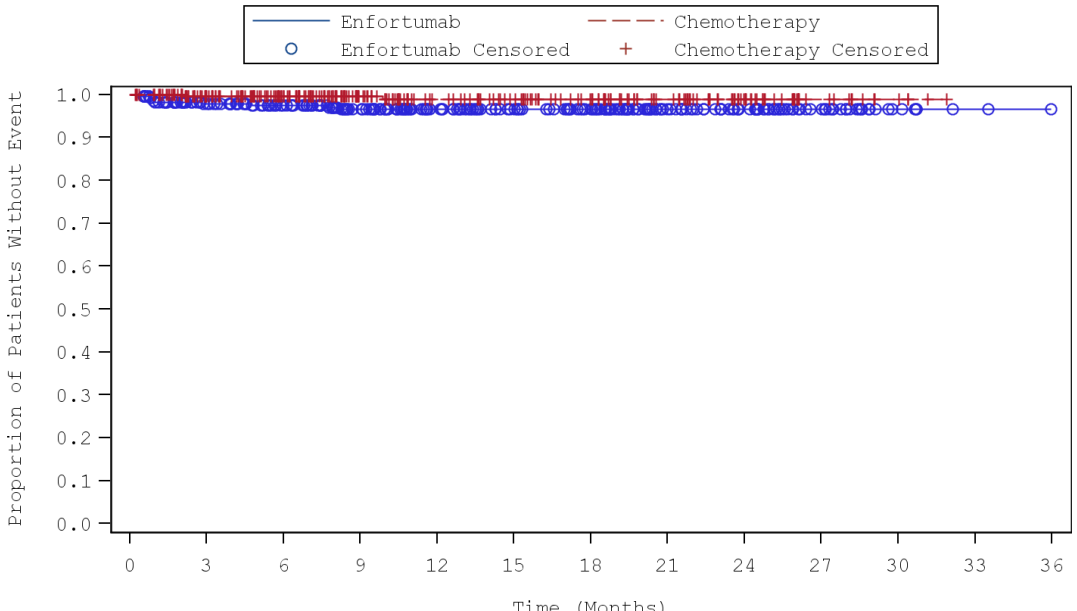
Enfortumab:	296	262	229	189	154	129	112	66	46	22	4	1	0
Chemotherapy:	291	248	206	148	119	104	86	62	38	14	6	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): NA (NA, NA)
P-value: 0.00102

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 sensorimotor neuropathy (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

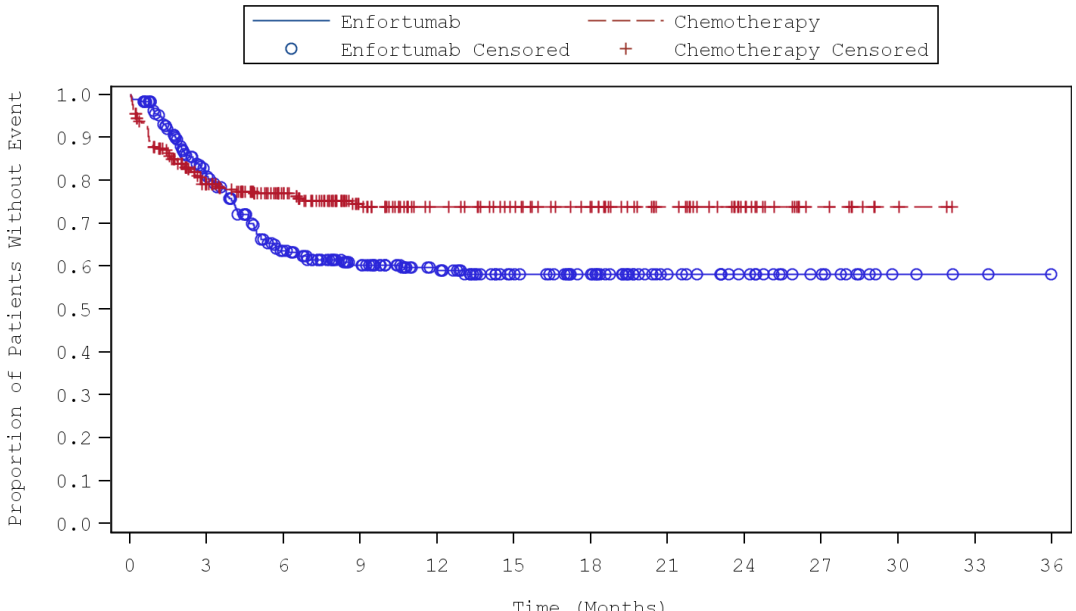
Enfortumab:	296	257	227	192	157	133	116	73	52	26	7	2	0
Chemotherapy:	291	247	205	148	118	103	85	61	37	13	5	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 4.144 (0.894, 19.204)
P-value: 0.04853

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

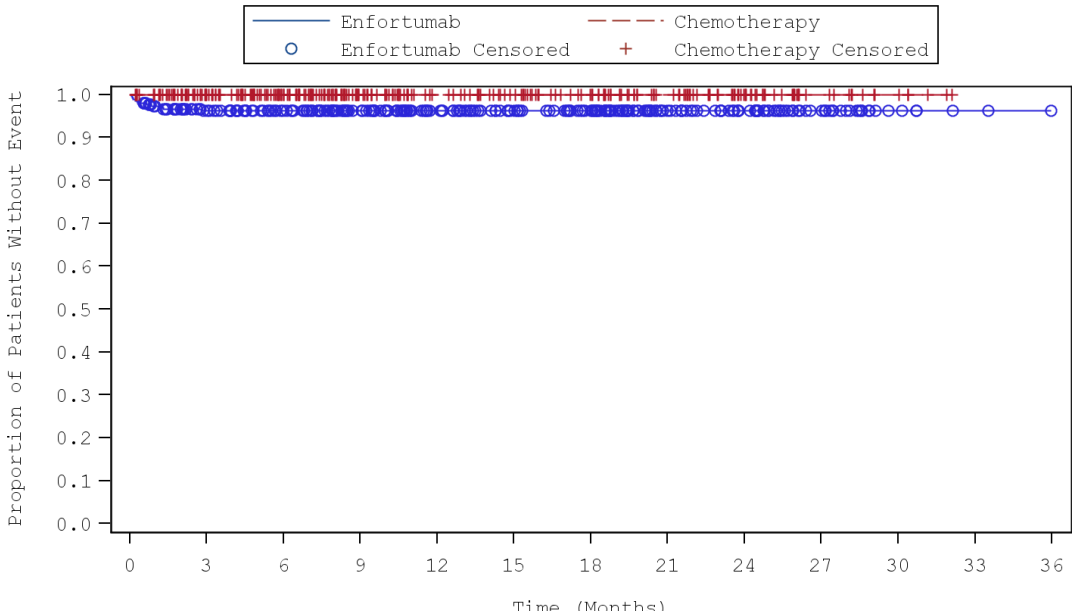
Enfortumab:	296	210	144	109	83	62	51	30	22	13	4	2	0
Chemotherapy:	291	192	148	101	77	66	55	39	24	10	3	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 1.421 (1.046, 1.931)
P-value: 0.02328

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

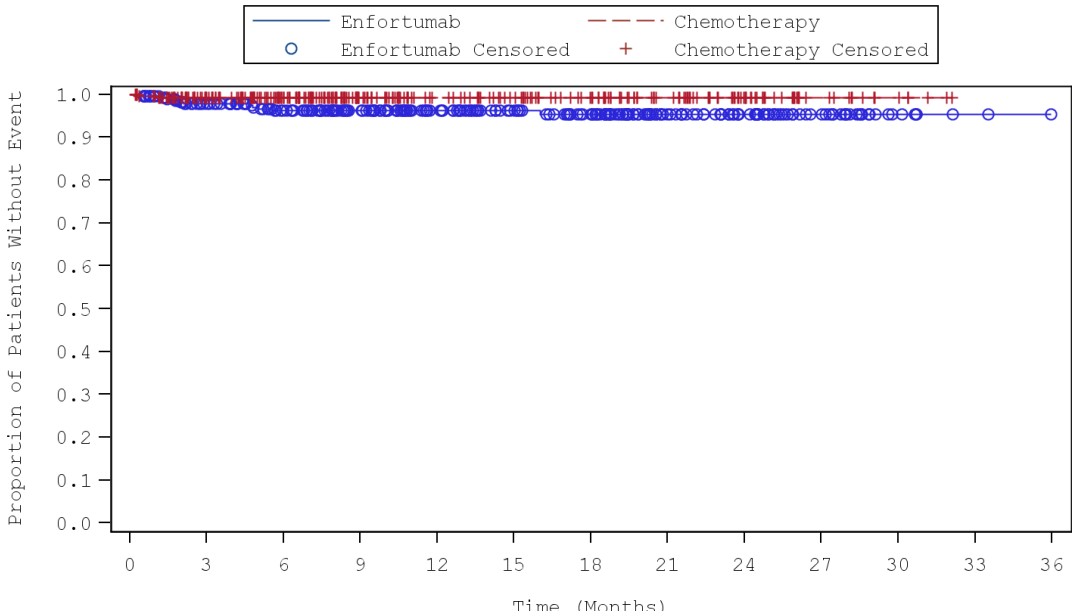
Enfortumab:	296	253	224	190	156	132	115	68	48	23	6	2	0
Chemotherapy:	291	248	206	148	119	104	86	62	38	14	6	0	0

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) - Psychiatric disorders: Depression (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

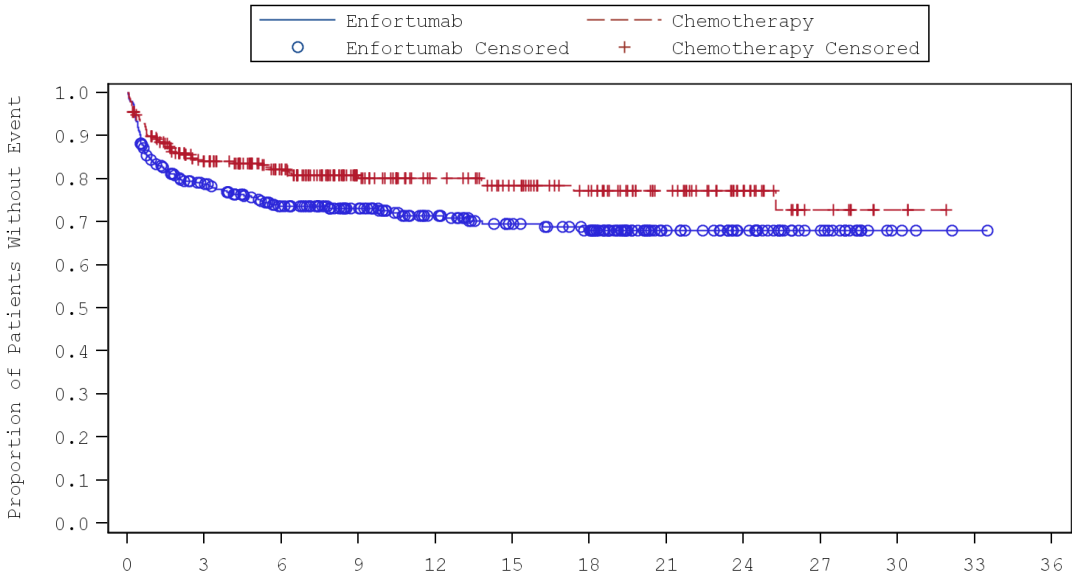
Enfortumab:	296	257	224	191	156	132	115	71	50	26	7	2	0
Chemotherapy:	291	248	206	148	119	104	86	62	38	14	6	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 5.149 (1.139, 23.272)
P-value: 0.01762

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

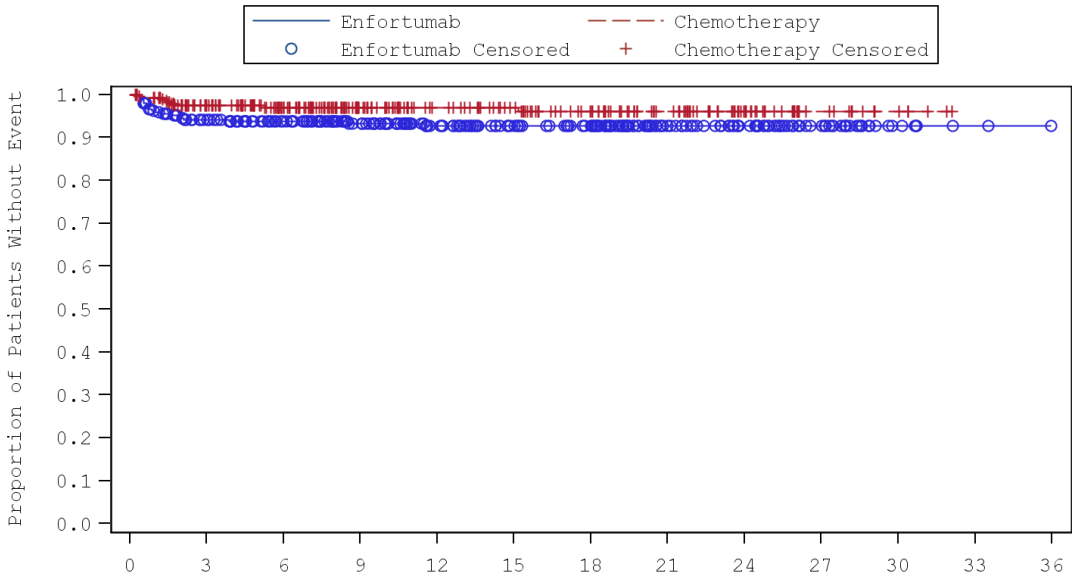
Enfortumab:	296	212	175	144	117	98	88	49	36	19	4	1	0
Chemotherapy:	291	212	176	122	97	83	67	47	27	9	3	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 1.458 (1.040, 2.045)
P-value: 0.02759

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

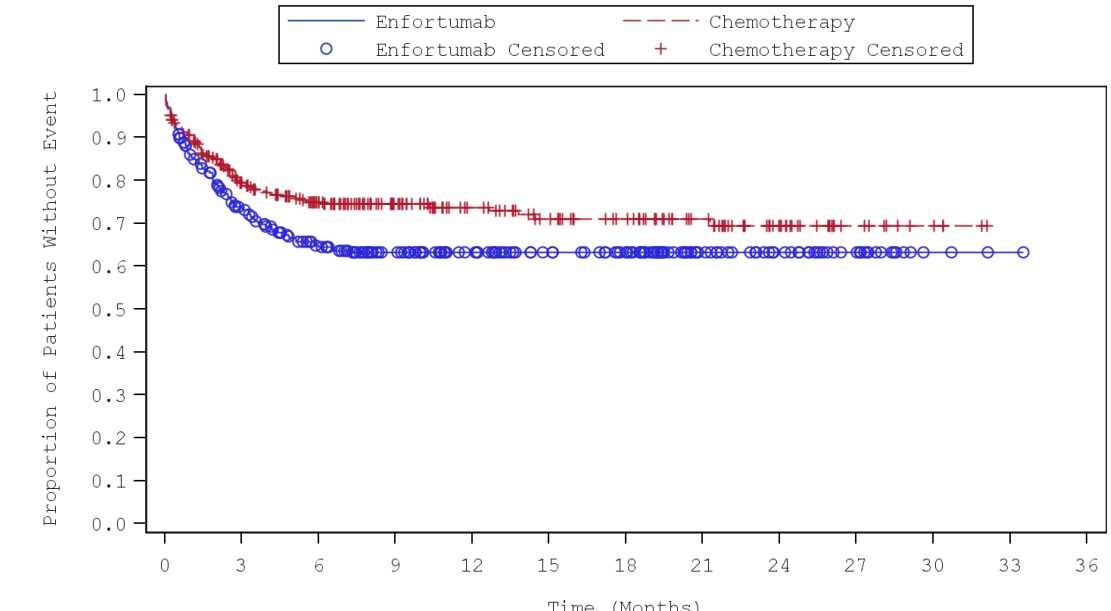
Enfortumab:	296	253	224	188	154	130	117	70	51	27	7	2	0
Chemotherapy:	291	245	204	147	118	103	84	61	37	14	6	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 2.168 (0.986, 4.766)
P-value: 0.04828

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

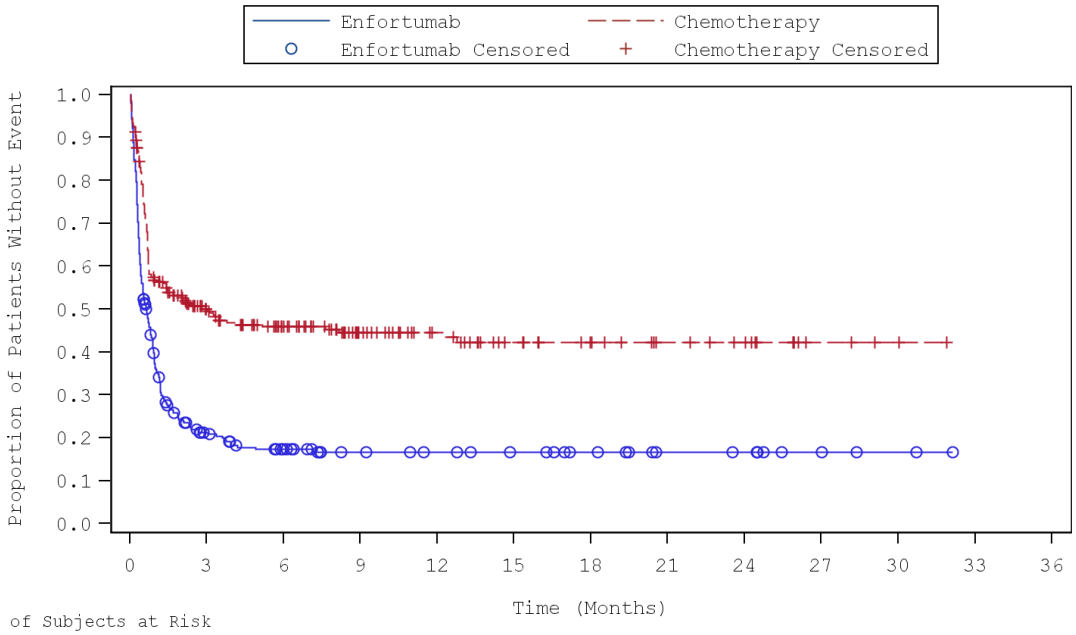
Enfortumab:	296	198	154	126	104	87	77	44	30	17	3	1	0
Chemotherapy:	291	199	159	115	90	75	64	46	27	11	5	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 1.381 (1.022, 1.865)
P-value: 0.03480

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



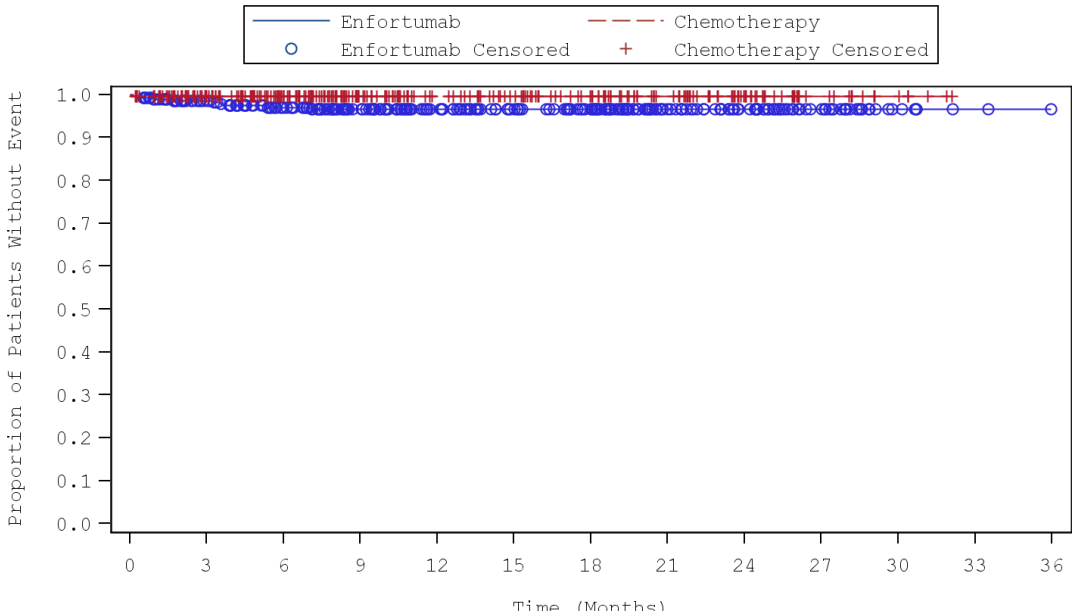
No. of Subjects at Risk

Enfortumab:	296	51	34	24	21	18	14	9	8	4	2	0	0
Chemotherapy:	291	114	85	55	40	28	22	16	13	4	2	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 2.158 (1.755, 2.653)
P-value: <.00001
Enfortumab Median (95% CI): 0.62 (0.49, 0.79)
Chemotherapy Median (95% CI): 2.86 (1.41, 12.22)

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

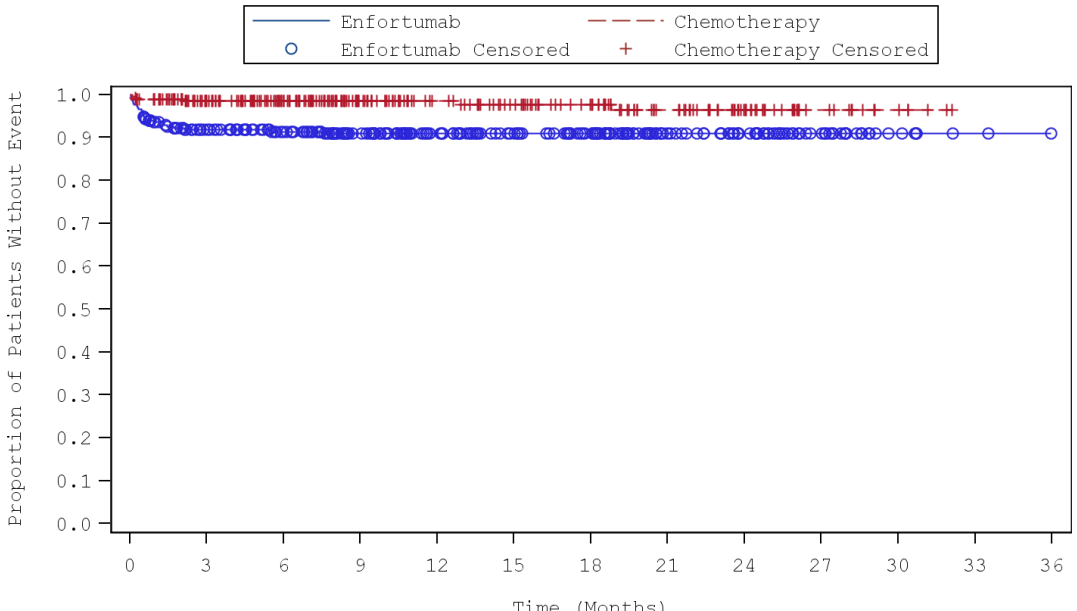
Enfortumab:	296	260	227	191	158	136	119	73	52	27	7	2	0
Chemotherapy:	291	247	205	147	119	104	86	62	38	14	6	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 8.893 (1.126, 70.208)
P-value: 0.01206

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

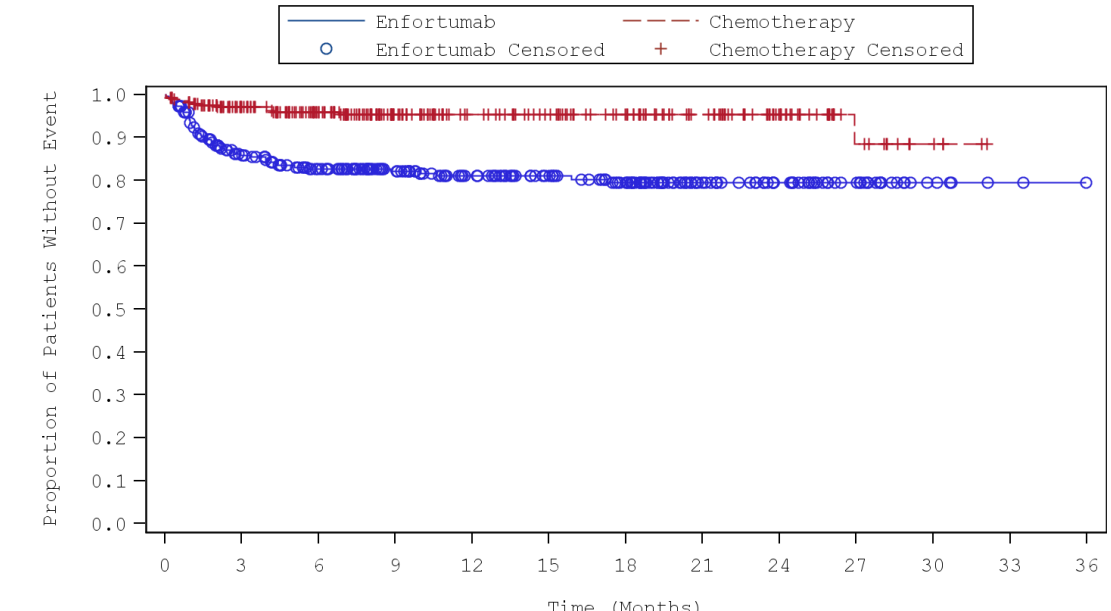
Enfortumab:	296	241	213	177	145	123	106	64	47	24	7	2	0
Chemotherapy:	291	244	202	145	117	101	84	59	38	14	6	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 4.690 (1.922, 11.444)
P-value: 0.00019

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

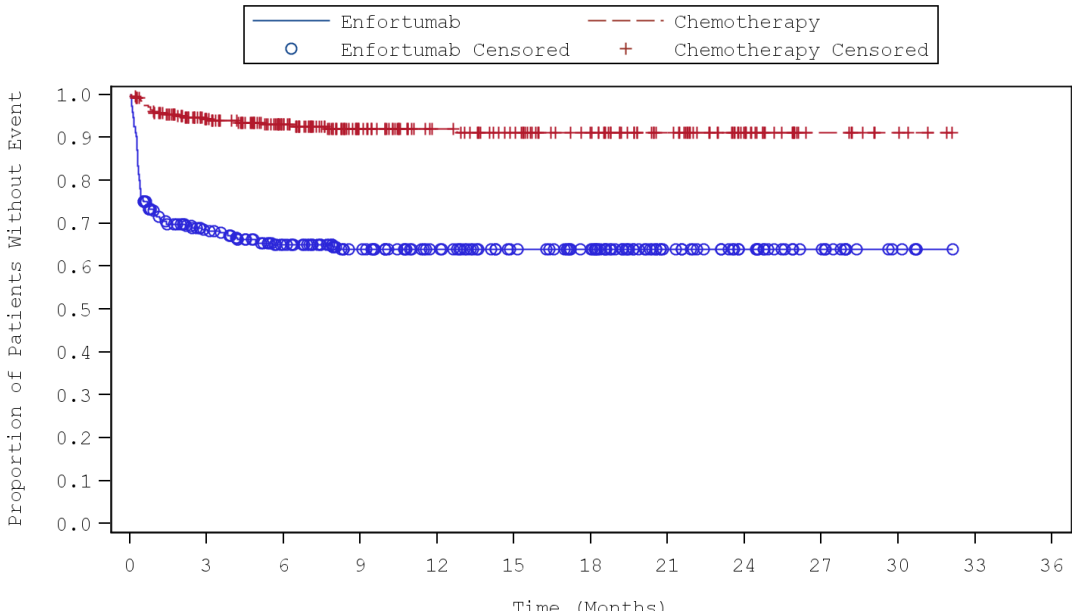
Enfortumab:	296	224	190	156	131	112	95	55	39	22	6	2	0
Chemotherapy:	291	241	197	142	113	99	82	60	37	13	5	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 4.271 (2.319, 7.867)
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

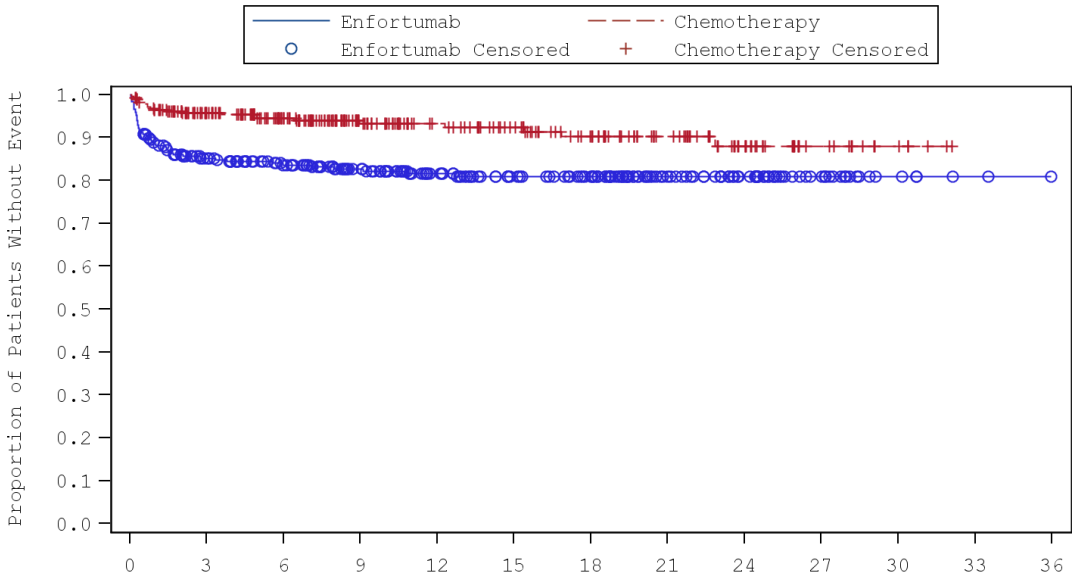
Enfortumab:	296	179	147	120	100	83	73	43	29	16	5	0	0
Chemotherapy:	291	233	189	133	106	92	76	55	32	11	5	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 5.820 (3.663, 9.248)
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

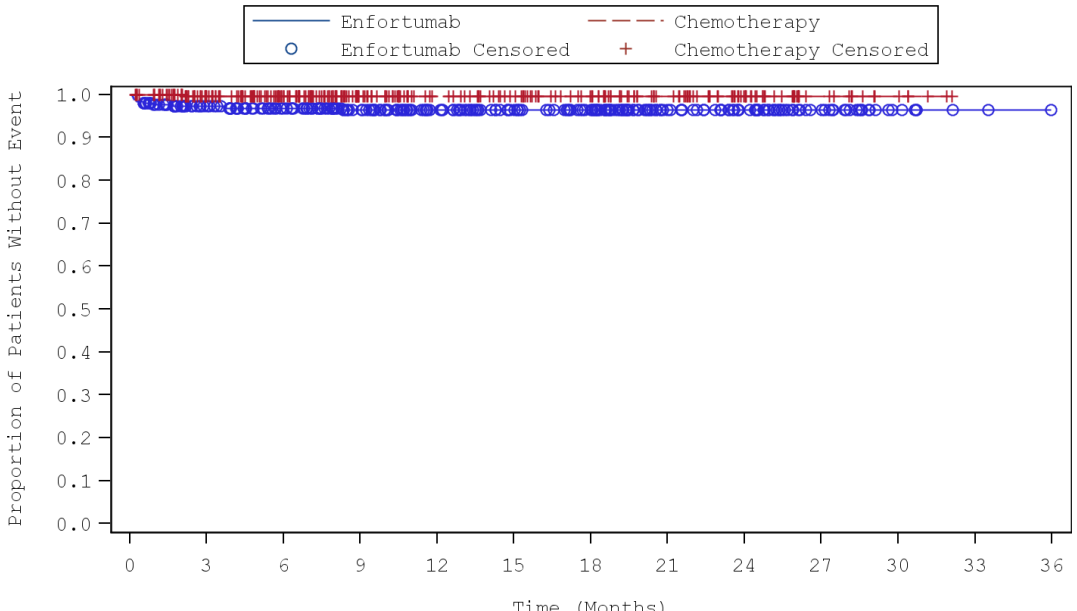
Enfortumab:	296	223	193	160	130	109	96	59	41	19	6	2	0
Chemotherapy:	291	236	194	137	110	94	74	53	33	14	6	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 2.546 (1.532, 4.231)
P-value: 0.00019

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

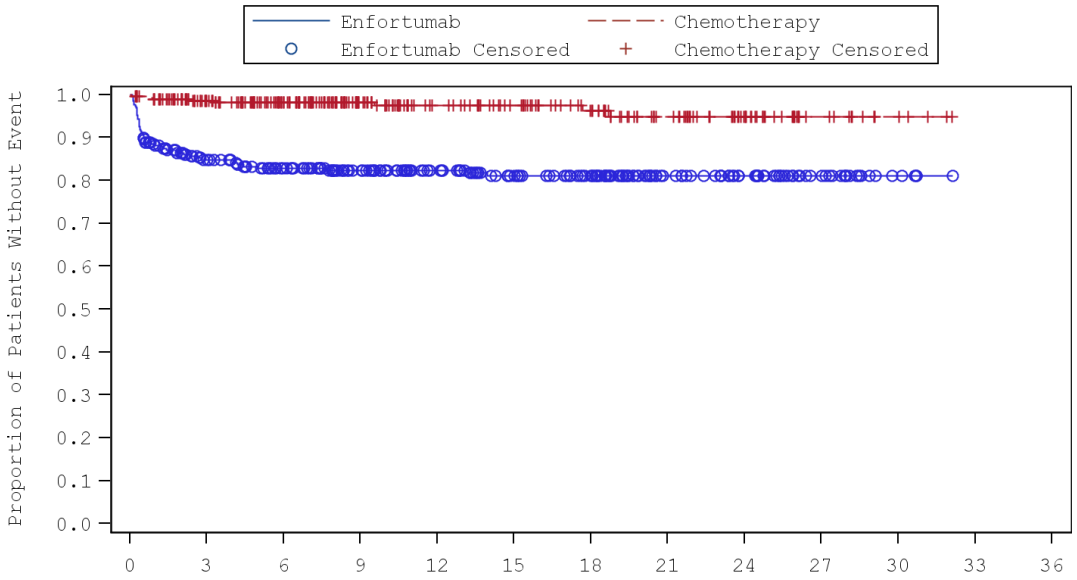
Enfortumab:	296	255	225	191	157	132	115	69	50	24	7	2	0
Chemotherapy:	291	247	205	148	119	104	86	62	38	14	6	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 9.685 (1.238, 75.764)
P-value: 0.00792

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

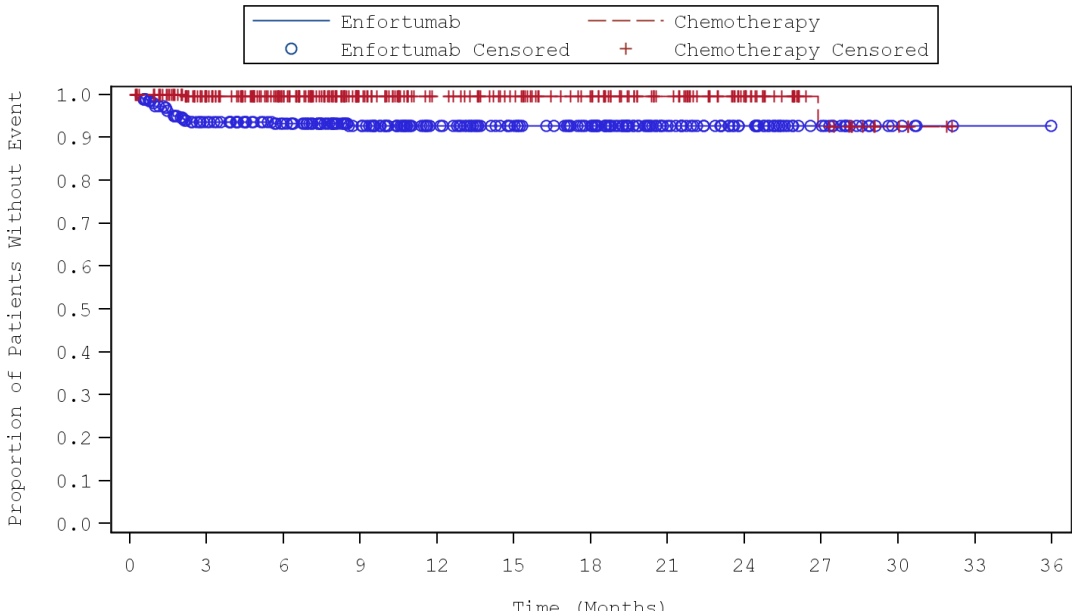
Enfortumab:	296	222	192	161	134	112	96	57	41	20	5	0	0
Chemotherapy:	291	244	201	143	113	98	80	57	36	13	5	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 7.210 (3.410, 15.246)
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	217	181	146	125	109	66	45	22	5	1	0
Chemotherapy:	291	247	205	147	118	103	86	62	38	13	5	0	0

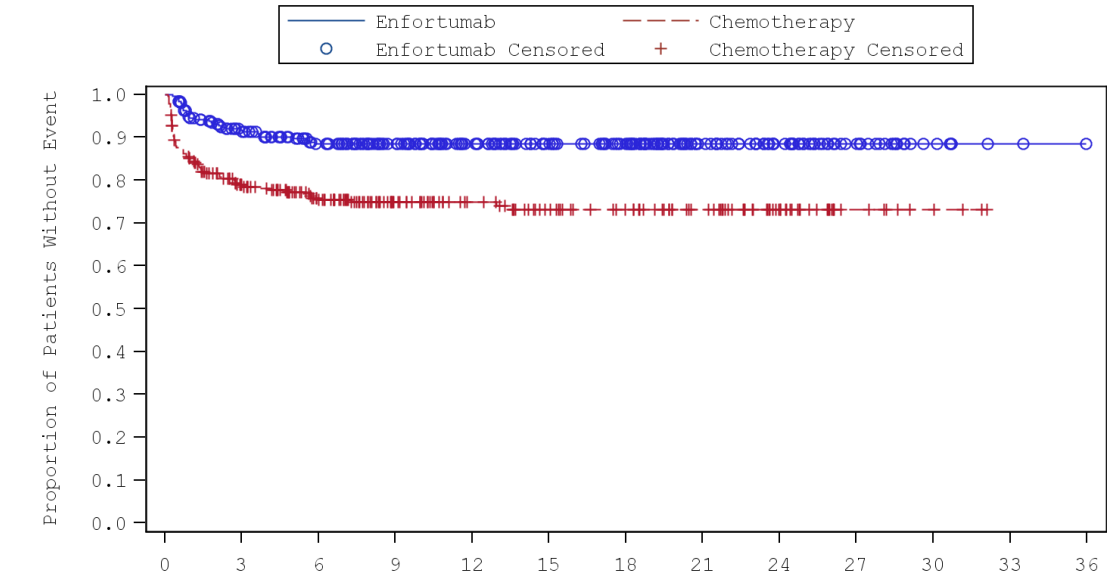
Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 10.886 (2.535, 46.745)
P-value: 0.00006

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

3.1.2 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

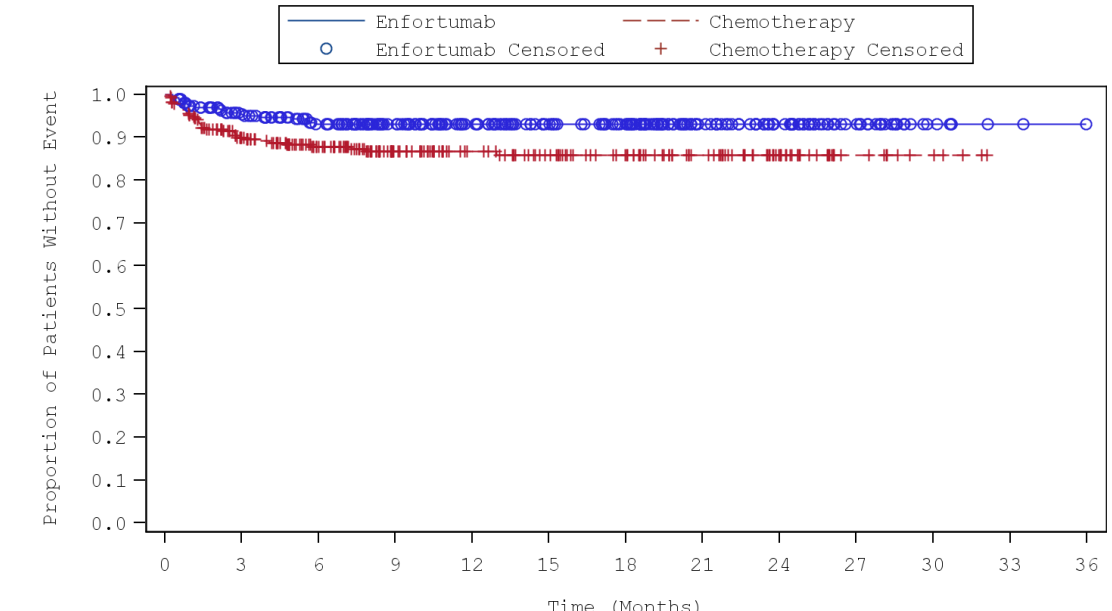
Enfortumab:	296	245	211	181	149	125	109	67	45	22	7	2	0
Chemotherapy:	291	200	160	114	92	76	65	50	29	9	4	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.378 (0.248, 0.575)
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

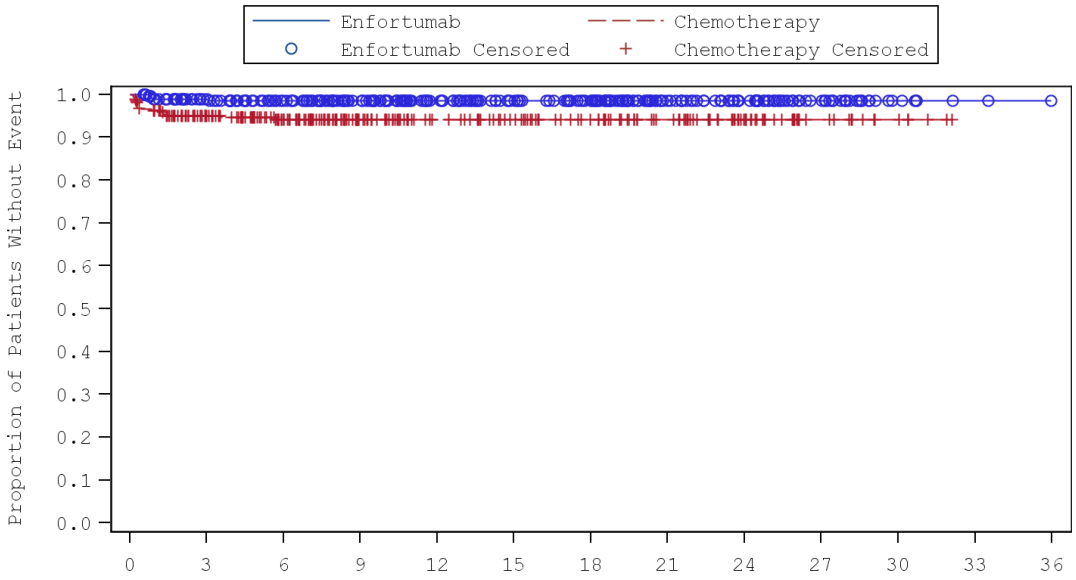
Enfortumab:	296	256	224	190	158	133	117	73	51	26	7	2	0
Chemotherapy:	291	226	183	133	107	91	75	55	33	11	5	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.470 (0.268, 0.823)
P-value: 0.00691

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

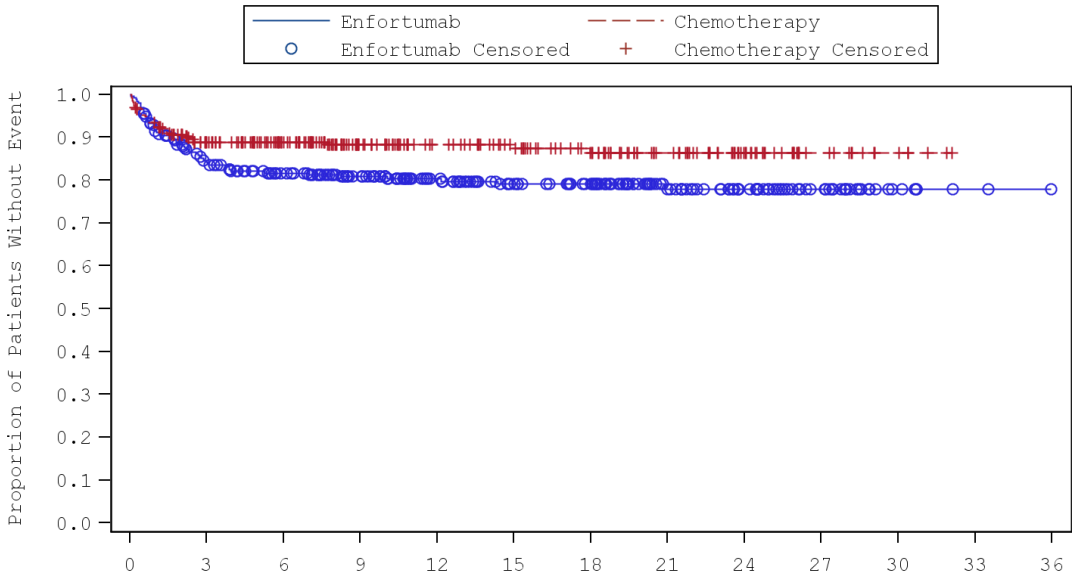
Enfortumab:	296	261	232	199	164	139	122	75	53	27	7	2	0
Chemotherapy:	291	236	195	139	111	97	81	61	38	14	6	0	0

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

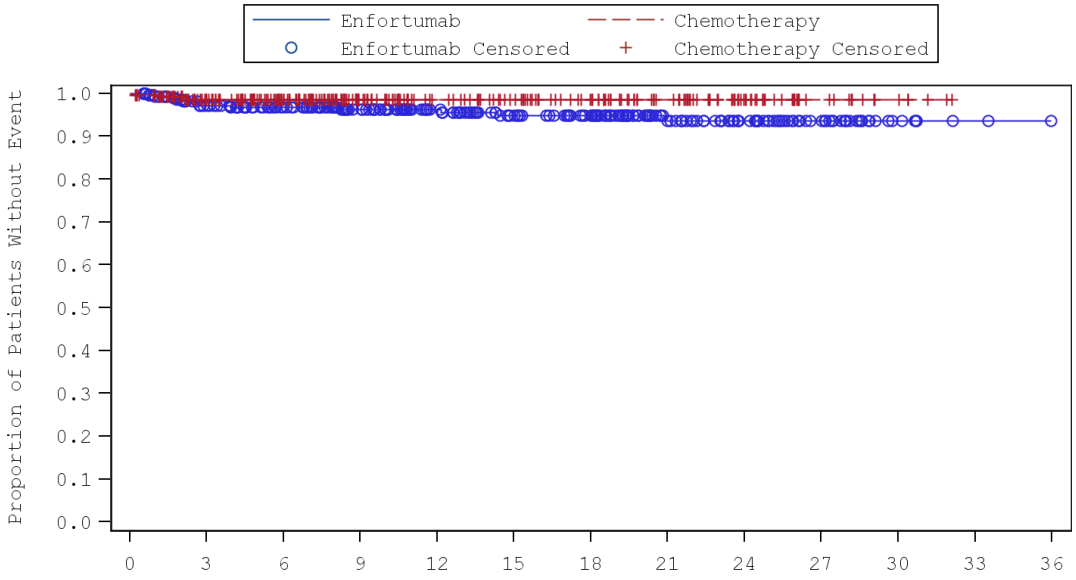
Enfortumab:	296	229	201	172	140	116	104	64	45	25	7	2	0
Chemotherapy:	291	229	191	140	115	99	82	58	36	14	6	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 1.624 (1.067, 2.473)
P-value: 0.02222

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: Urinary tract infection bacterial (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

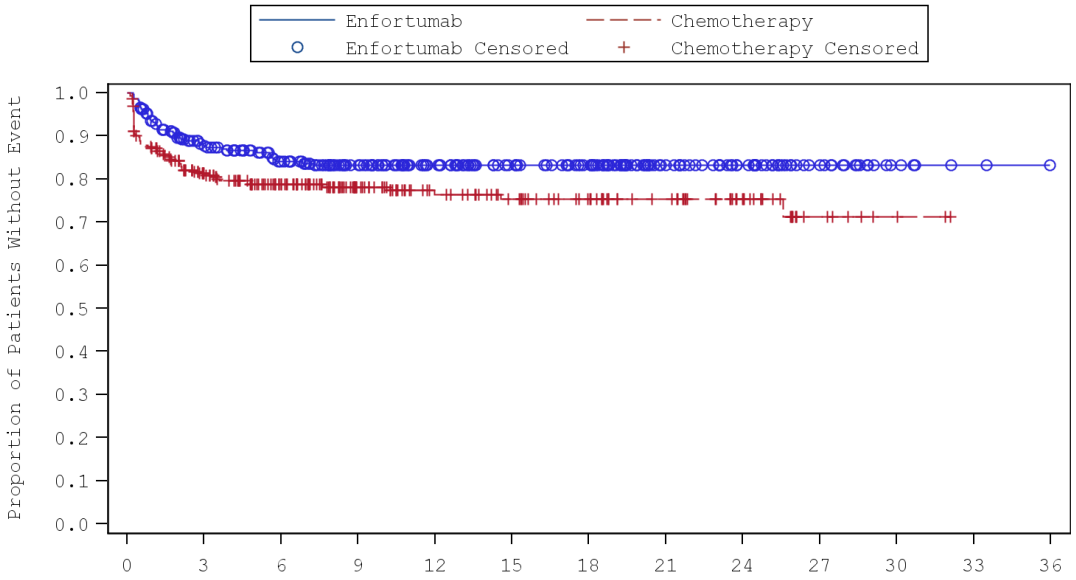
Enfortumab:	296	257	227	193	159	133	117	73	51	27	7	2	0
Chemotherapy:	291	246	204	147	118	103	85	61	37	14	6	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 3.066 (0.998, 9.420)
P-value: 0.03946

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 (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

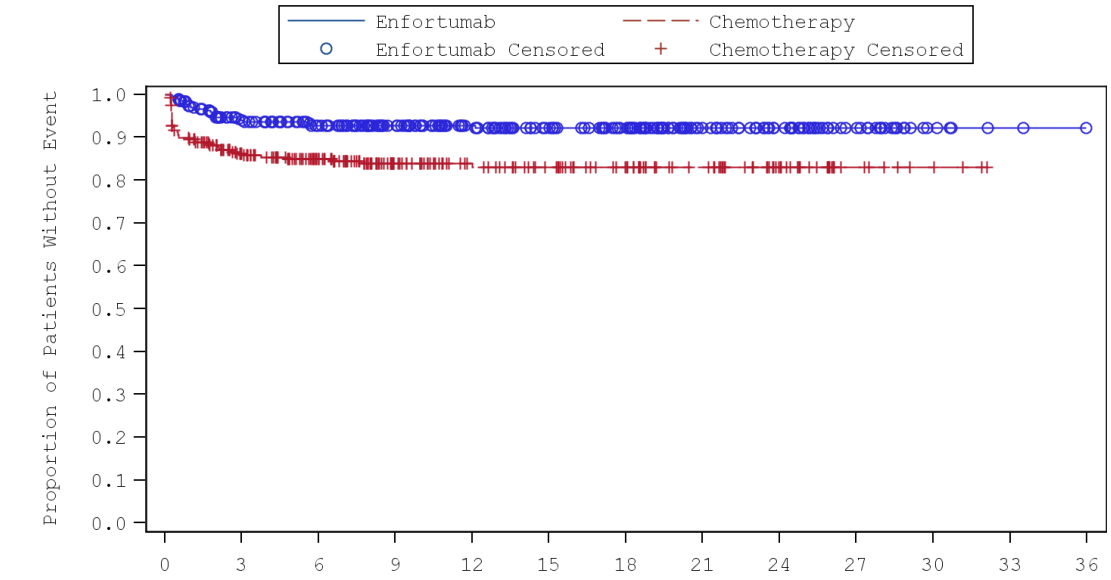
Enfortumab:	296	231	197	164	134	112	97	58	41	20	6	2	0
Chemotherapy:	291	200	159	109	83	70	57	43	27	8	3	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.612 (0.418, 0.898)
P-value: 0.01220

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

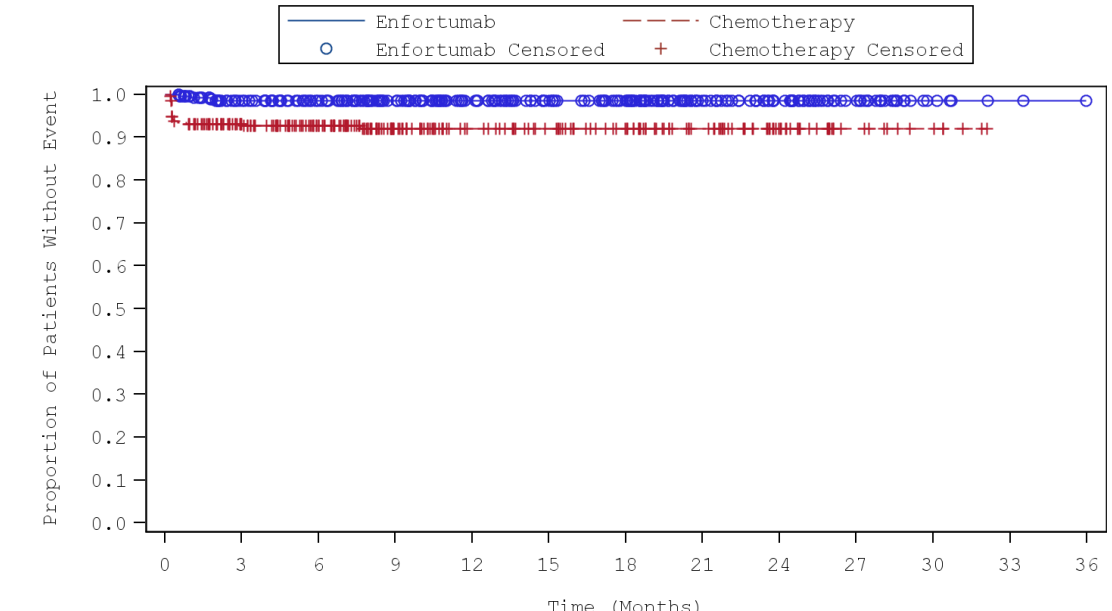
Enfortumab:	296	248	217	183	152	128	111	68	48	24	6	2	0
Chemotherapy:	291	211	171	118	93	80	65	48	29	9	4	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.385 (0.228, 0.649)
P-value: 0.00022

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

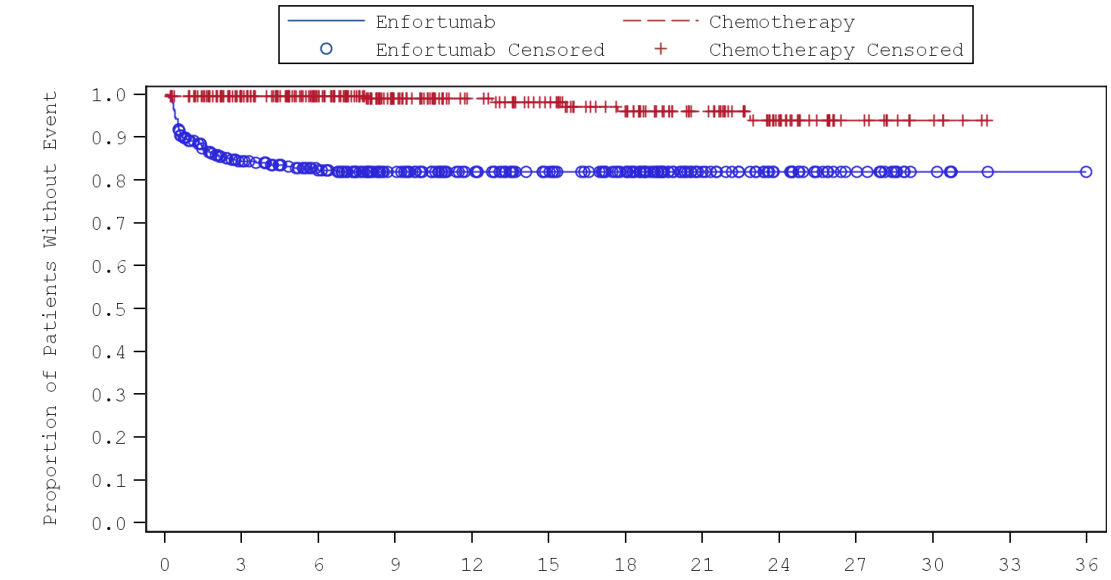
Enfortumab:	296	259	231	197	162	137	120	74	52	26	6	2	0
Chemotherapy:	291	229	191	136	108	94	78	55	32	12	6	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 0.157 (0.053, 0.462)
P-value: 0.00013

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

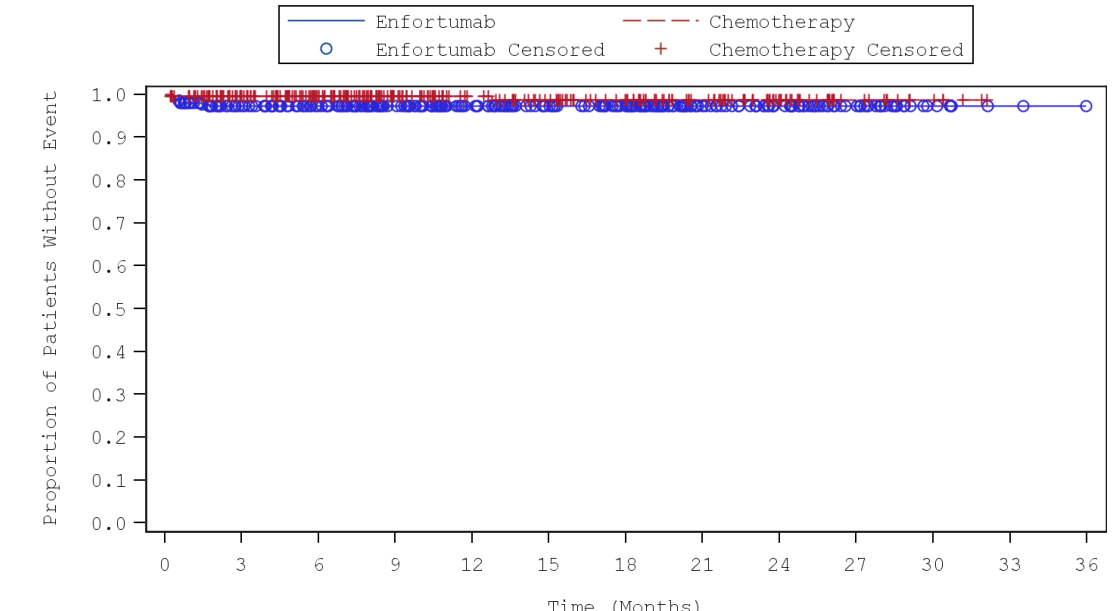
Enfortumab:	296	221	190	155	130	112	95	53	36	19	6	1	0
Chemotherapy:	291	247	205	146	117	102	83	60	37	14	6	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 9.370 (3.998, 21.960)
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: Drug eruption (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

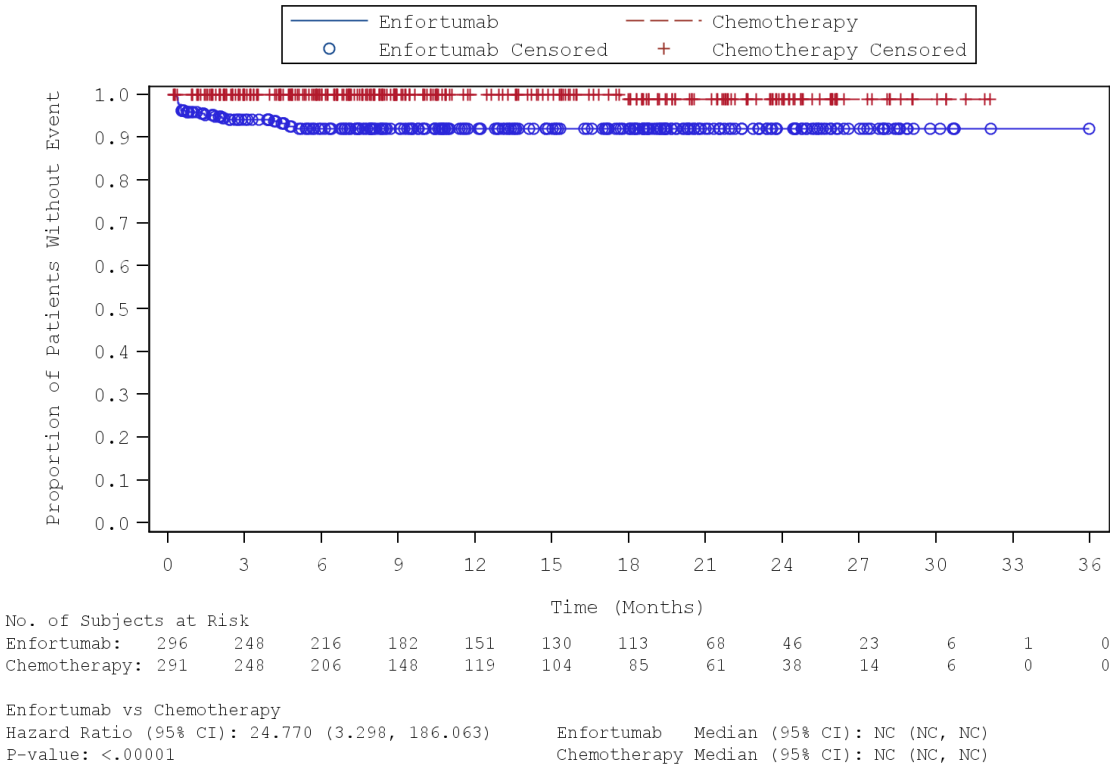
Enfortumab:	296	256	227	192	159	135	118	71	51	27	7	2	0
Chemotherapy:	291	247	205	147	118	102	85	61	38	14	6	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 4.426 (0.933, 20.989)
P-value: 0.04095

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

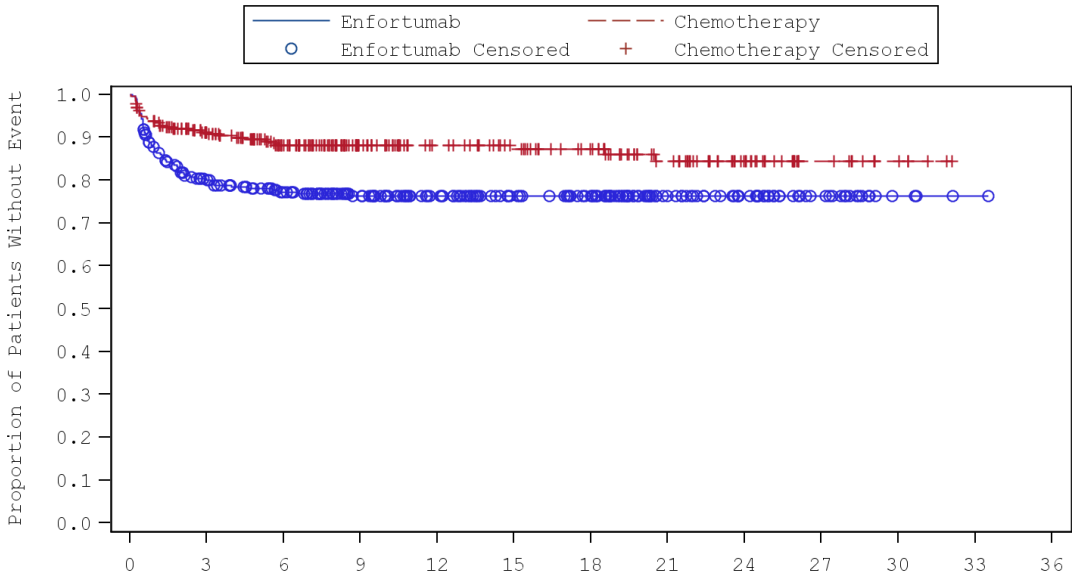
Enfortumab:	296	248	216	182	151	130	113	68	46	23	6	1	0
Chemotherapy:	291	248	206	148	119	104	85	61	38	14	6	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 24.770 (3.298, 186.063)
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

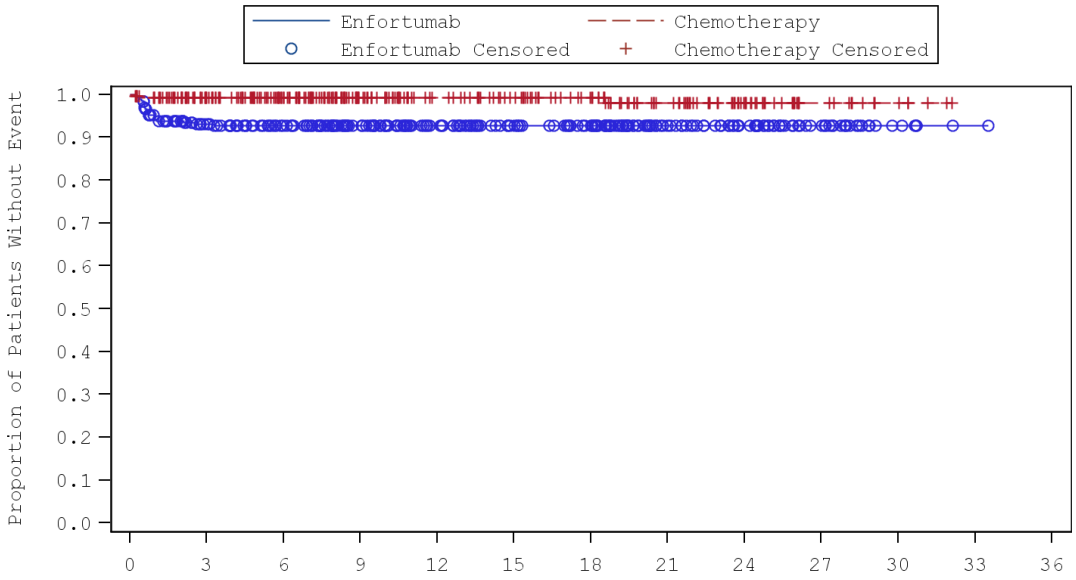
Enfortumab:	296	215	186	154	127	104	92	53	37	18	4	1	0
Chemotherapy:	291	228	183	129	104	90	77	54	33	13	6	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 1.906 (1.265, 2.871)
P-value: 0.00167

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

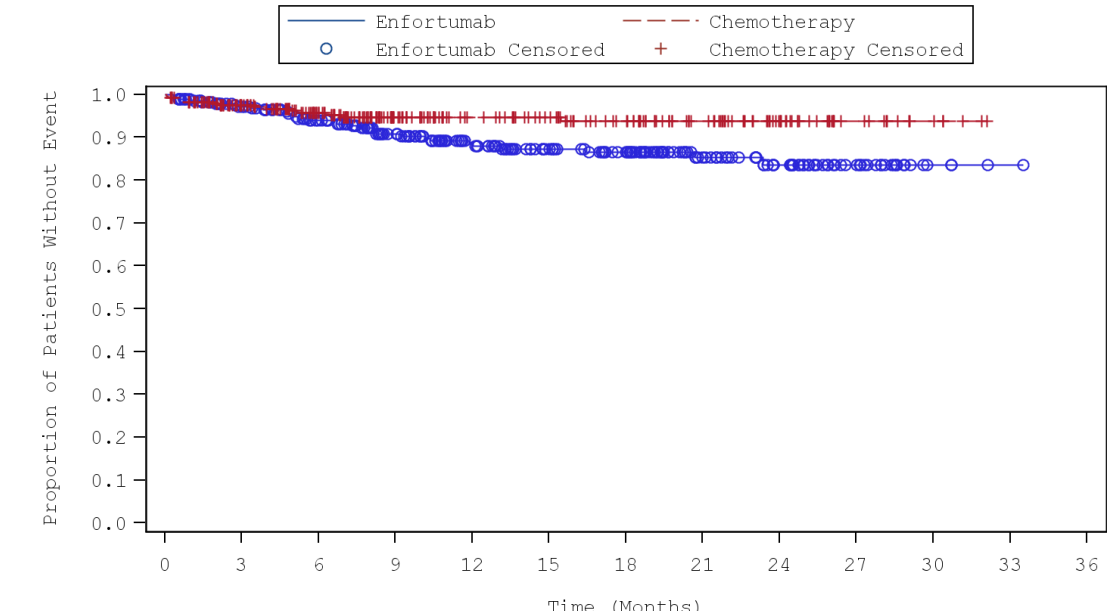
Enfortumab:	296	246	219	185	152	128	113	68	48	24	6	1	0
Chemotherapy:	291	247	206	148	119	104	86	61	37	14	6	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 6.931 (2.066, 23.248)
P-value: 0.00027

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) - Nervous system disorders (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

Enfortumab:	296	259	223	183	146	119	103	63	44	22	4	1	0
Chemotherapy:	291	242	197	140	112	99	82	59	36	14	6	0	0

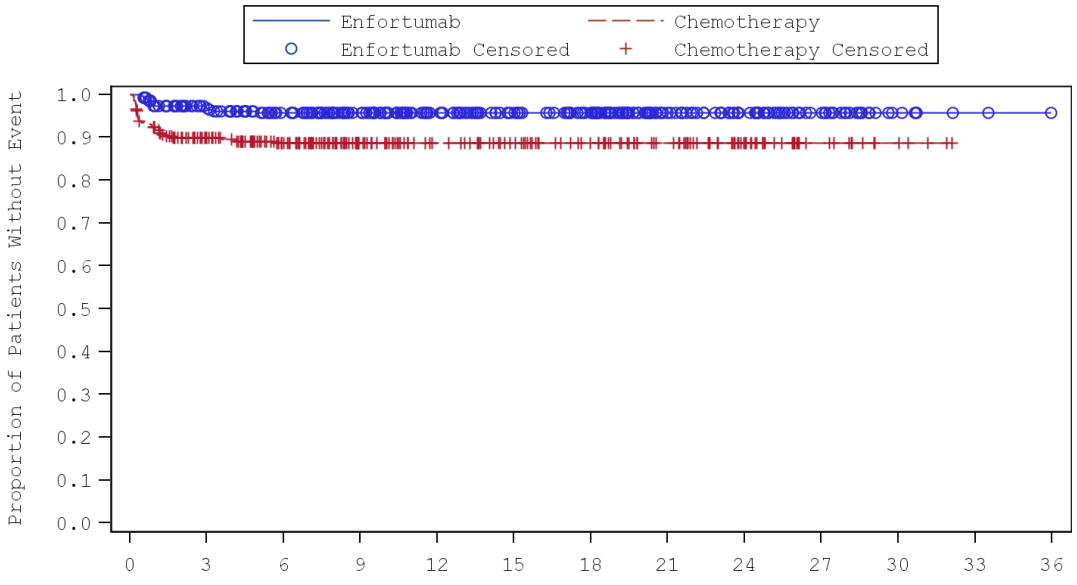
Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 2.027 (1.076, 3.818)
P-value: 0.02560

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

3.1.3 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

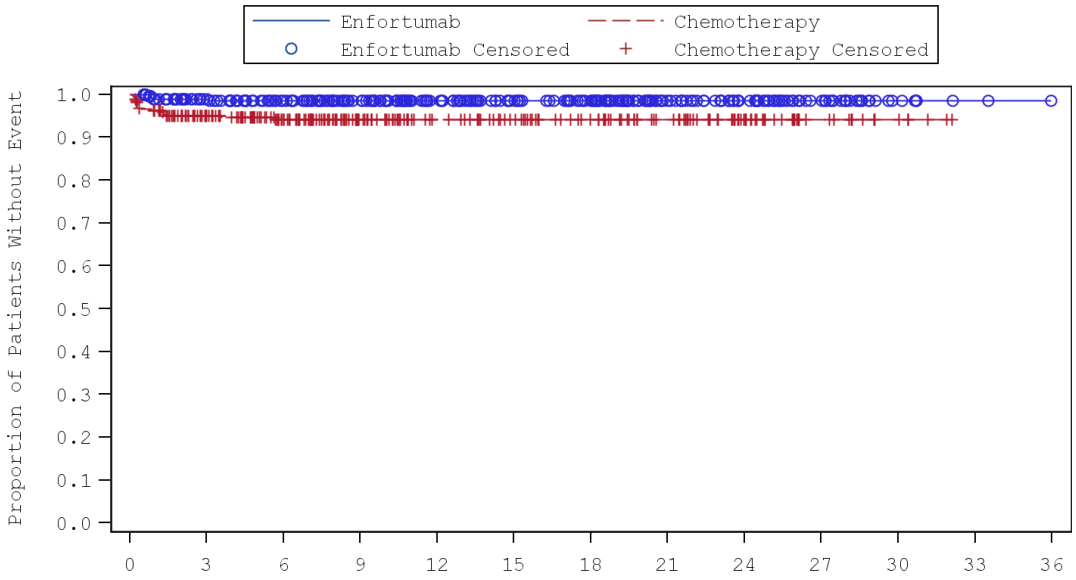
Enfortumab:	296	256	226	194	160	136	119	73	51	26	7	2	0
Chemotherapy:	291	226	188	133	109	95	79	60	37	13	5	0	0

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

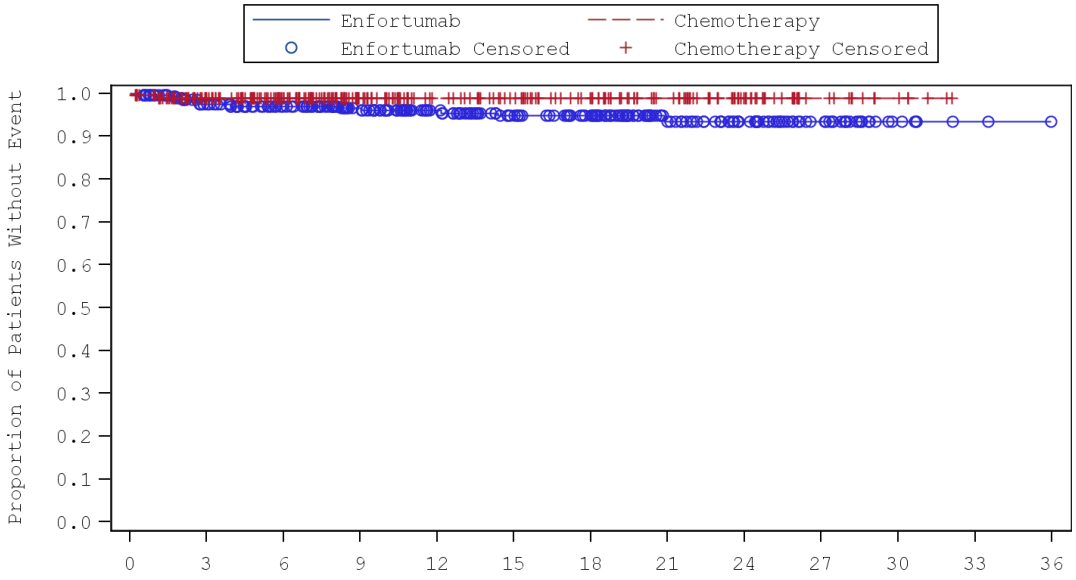
Enfortumab:	296	261	232	199	164	139	122	75	53	27	7	2	0
Chemotherapy:	291	236	195	139	111	97	81	61	38	14	6	0	0

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) - Infections and infestations: Urinary tract infection bacterial (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

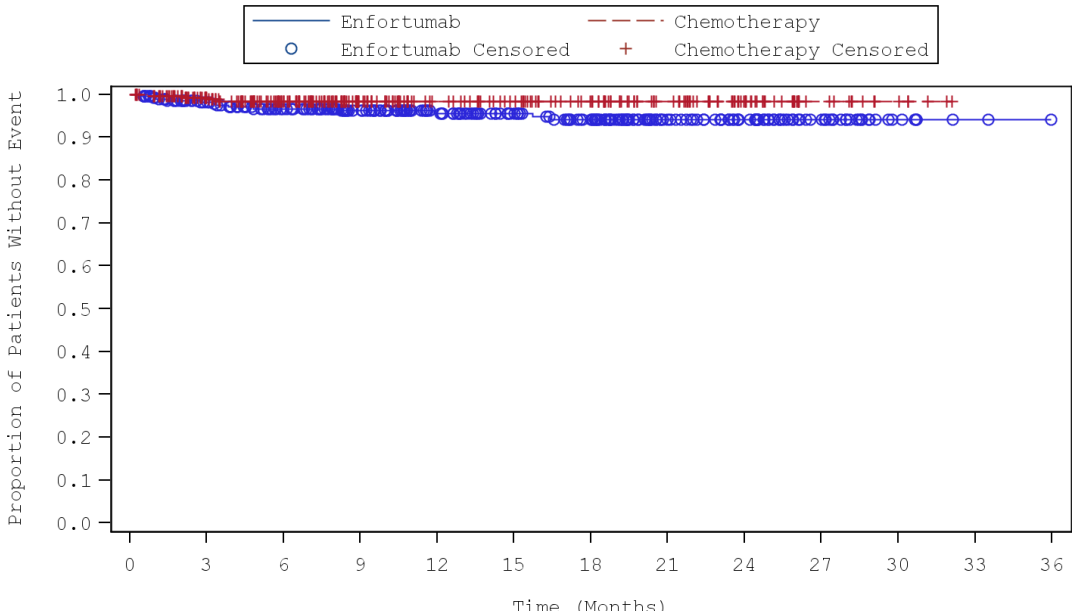
Enfortumab:	296	257	227	193	158	131	115	71	50	26	7	2	0
Chemotherapy:	291	247	205	147	118	103	85	61	37	14	6	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 3.967 (1.128, 13.954)
P-value: 0.02040

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) - Nervous system disorders (Safety Analysis Set)
Subgroup: Overall, Level: NA



No. of Subjects at Risk

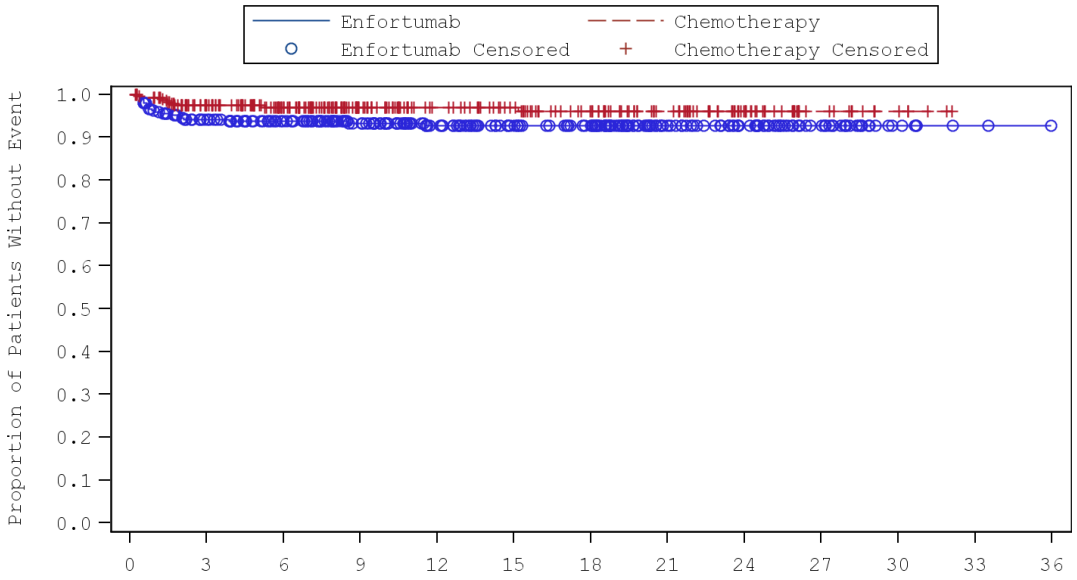
Enfortumab:	296	261	229	194	159	135	117	71	51	26	7	2	0
Chemotherapy:	291	246	203	147	118	104	86	62	38	14	6	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 2.965 (0.966, 9.105)
P-value: 0.04628

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

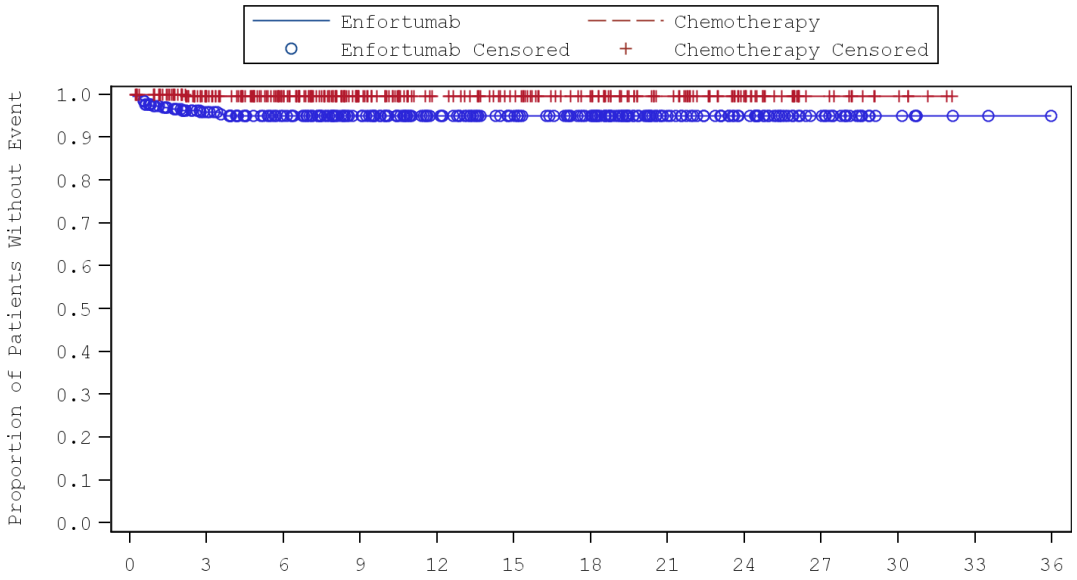
Enfortumab:	296	253	224	188	154	130	117	70	51	27	7	2	0
Chemotherapy:	291	245	204	147	118	103	84	61	37	14	6	0	0

Enfortumab vs Chemotherapy
Hazard Ratio (95% CI): 2.168 (0.986, 4.766)
P-value: 0.04828

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	222	188	154	133	116	70	50	25	7	2	0
Chemotherapy:	291	247	206	148	119	104	86	62	38	14	6	0	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

3.2 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]		0.918 (0.776, 1.086)
	Treatment P-value [b]		0.39237
	Homogeneity P-value [c]		0.00995
Blood and lymphatic system disorders	No. of Events (%)	87 (29.4)	128 (44.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (7.06, NC)
	Hazard Ratio (95% CI) [a]		0.563 (0.427, 0.741)
	Treatment P-value [b]		0.00003
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	62 (20.9)	91 (31.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.606 (0.438, 0.839)
	Treatment P-value [b]		0.00234
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
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)	29 (10.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.642 (0.363, 1.136)
	Treatment P-value [b]		0.12506
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Thrombocytopenia	No. of Events (%)	11 (3.7)	7 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.468 (0.567, 3.801)
	Treatment P-value [b]		0.42663
	Homogeneity P-value [c]		NA
Cardiac disorders	No. of Events (%)	25 (8.4)	16 (5.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.537 (0.820, 2.882)
	Treatment P-value [b]		0.17668
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Ear and labyrinth disorders	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]		1.925 (0.664, 5.585)
	Treatment P-value [b]		0.22007
	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]		0.954 (0.312, 2.923)
	Treatment P-value [b]		0.93471
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Eye disorders	No. of Events (%)	86 (29.1)	26 (8.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.671 (2.364, 5.701)
	Treatment P-value [b]		<.00001
	Homogeneity P-value [c]		NA
Cataract	No. of Events (%)	10 (3.4)	2 (0.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.128 (0.895, 19.039)
	Treatment P-value [b]		0.04907
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Dry eye	No. of Events (%)	20 (6.8)	3 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.405 (1.902, 21.571)
	Treatment P-value [b]		0.00057
	Homogeneity P-value [c]		NA
Lacrimation increased	No. of Events (%)	34 (11.5)	12 (4.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.721 (1.406, 5.266)
	Treatment P-value [b]		0.00197
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Vision blurred	No. of Events (%)	17 (5.7)	5 (1.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.386 (1.246, 9.202)
	Treatment P-value [b]		0.01110
	Homogeneity P-value [c]		NA
Gastrointestinal disorders	No. of Events (%)	211 (71.3)	188 (64.6)
	Median Survival Est. (95% CI)	0.82 (0.62, 1.22)	1.35 (0.72, 2.00)
	Hazard Ratio (95% CI) [a]		1.064 (0.872, 1.298)
	Treatment P-value [b]		0.51298
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Abdominal pain	No. of Events (%)	42 (14.2)	29 (10.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.399 (0.871, 2.248)
	Treatment P-value [b]		0.16502
	Homogeneity P-value [c]		NA
Abdominal pain lower	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]		3.722 (0.789, 17.554)
	Treatment P-value [b]		0.07473
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Abdominal pain upper	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]		1.568 (0.649, 3.789)
	Treatment P-value [b]		0.31145
	Homogeneity P-value [c]		NA
Constipation	No. of Events (%)	85 (28.7)	80 (27.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (28.09, NC)
	Hazard Ratio (95% CI) [a]		1.006 (0.740, 1.369)
	Treatment P-value [b]		0.94823
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Diarrhoea	No. of Events (%)	106 (35.8)	70 (24.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.566 (1.156, 2.121)
	Treatment P-value [b]		0.00364
	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

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	20 (6.8)	10 (3.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.959 (0.915, 4.197)
	Treatment P-value [b]		0.07768
	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]		1.353 (0.381, 4.812)
	Treatment P-value [b]		0.63899
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Nausea	No. of Events (%)	95 (32.1)	78 (26.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.161 (0.860, 1.569)
	Treatment P-value [b]		0.32874
	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

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Vomiting	No. of Events (%)	44 (14.9)	47 (16.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.894 (0.591, 1.350)
	Treatment P-value [b]		0.58952
	Homogeneity P-value [c]		NA
General disorders and administration site conditions	No. of Events (%)	217 (73.3)	191 (65.6)
	Median Survival Est. (95% CI)	1.25 (0.85, 1.68)	1.18 (0.79, 2.07)
	Hazard Ratio (95% CI) [a]		1.078 (0.886, 1.311)
	Treatment P-value [b]		0.43717
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Asthenia	No. of Events (%)	49 (16.6)	42 (14.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.033 (0.682, 1.564)
	Treatment P-value [b]		0.86948
	Homogeneity P-value [c]		NA
Chills	No. of Events (%)	20 (6.8)	6 (2.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.117 (1.250, 7.771)
	Treatment P-value [b]		0.01013
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Fatigue	No. of Events (%)	110 (37.2)	81 (27.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.341 (1.006, 1.789)
	Treatment P-value [b]		0.04535
	Homogeneity P-value [c]		NA
Gait disturbance	No. of Events (%)	10 (3.4)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00435
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
General physical health deterioration	No. of Events (%)	8 (2.7)	11 (3.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.660 (0.265, 1.647)
	Treatment P-value [b]		0.37010
	Homogeneity P-value [c]		NA
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

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Malaise	No. of Events (%)	13 (4.4)	23 (7.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.514 (0.260, 1.017)
	Treatment P-value [b]		0.05210
	Homogeneity P-value [c]		NA
Mucosal inflammation	No. of Events (%)	15 (5.1)	14 (4.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.024 (0.494, 2.122)
	Treatment P-value [b]		0.94953
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Oedema peripheral	No. of Events (%)	33 (11.1)	43 (14.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (28.32, NC)
	Hazard Ratio (95% CI) [a]		0.694 (0.440, 1.096)
	Treatment P-value [b]		0.11575
	Homogeneity P-value [c]		NA
Pain	No. of Events (%)	5 (1.7)	11 (3.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.432 (0.150, 1.245)
	Treatment P-value [b]		0.10967
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Pyrexia	No. of Events (%)	68 (23.0)	45 (15.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (29.73, NC)
	Hazard Ratio (95% CI) [a]		1.472 (1.006, 2.153)
	Treatment P-value [b]		0.04544
	Homogeneity P-value [c]		NA
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]		1.506 (0.652, 3.482)
	Treatment P-value [b]		0.33471
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Infections and infestations	No. of Events (%)	157 (53.0)	111 (38.1)
	Median Survival Est. (95% CI)	5.45 (3.48, 11.33)	NC (17.68, NC)
	Hazard Ratio (95% CI) [a]		1.451 (1.136, 1.853)
	Treatment P-value [b]		0.00276
	Homogeneity P-value [c]		NA
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

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Conjunctivitis	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]		6.569 (1.938, 22.272)
	Treatment P-value [b]		0.00051
	Homogeneity P-value [c]		NA
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

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Nasopharyngitis	No. of Events (%)	15 (5.1)	10 (3.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.435 (0.643, 3.199)
	Treatment P-value [b]		0.37499
	Homogeneity P-value [c]		NA
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

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Pneumonia	No. of Events (%)	22 (7.4)	12 (4.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.796 (0.888, 3.635)
	Treatment P-value [b]		0.09858
	Homogeneity P-value [c]		NA
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]		0.696 (0.258, 1.881)
	Treatment P-value [b]		0.47456
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Urinary tract infection	No. of Events (%)	28 (9.5)	21 (7.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.262 (0.714, 2.232)
	Treatment P-value [b]		0.42269
	Homogeneity P-value [c]		NA
Urinary tract infection bacterial	No. of Events (%)	24 (8.1)	13 (4.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.708 (0.868, 3.358)
	Treatment P-value [b]		0.11603
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Injury, poisoning and procedural complications	No. of Events (%)	45 (15.2)	34 (11.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (28.78, NC)
	Hazard Ratio (95% CI) [a]		1.263 (0.808, 1.976)
	Treatment P-value [b]		0.30289
	Homogeneity P-value [c]		NA
Fall	No. of Events (%)	20 (6.8)	9 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.040 (0.926, 4.493)
	Treatment P-value [b]		0.07068
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Infusion related reaction	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]		0.621 (0.240, 1.603)
	Treatment P-value [b]		0.32256
	Homogeneity P-value [c]		NA
Investigations	No. of Events (%)	141 (47.6)	124 (42.6)
	Median Survival Est. (95% CI)	10.38 (4.86, NC)	NC (10.38, NC)
	Hazard Ratio (95% CI) [a]		1.008 (0.790, 1.285)
	Treatment P-value [b]		0.92645
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Alanine aminotransferase increased	No. of Events (%)	27 (9.1)	7 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.766 (1.637, 8.666)
	Treatment P-value [b]		0.00083
	Homogeneity P-value [c]		NA
Amylase increased	No. of Events (%)	12 (4.1)	4 (1.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.859 (0.918, 8.899)
	Treatment P-value [b]		0.05825
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Aspartate aminotransferase increased	No. of Events (%)	36 (12.2)	6 (2.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.021 (2.533, 14.313)
	Treatment P-value [b]		<.00001
	Homogeneity P-value [c]		NA
Blood alkaline phosphatase increased	No. of Events (%)	9 (3.0)	11 (3.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.729 (0.300, 1.774)
	Treatment P-value [b]		0.48471
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Blood creatinine increased	No. of Events (%)	28 (9.5)	8 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (30.62, NC)
	Hazard Ratio (95% CI) [a]		4.118 (1.794, 9.454)
	Treatment P-value [b]		0.00030
	Homogeneity P-value [c]		NA
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

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Lymphocyte count decreased	No. of Events (%)	15 (5.1)	18 (6.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.818 (0.412, 1.626)
	Treatment P-value [b]		0.56580
	Homogeneity P-value [c]		NA
Neutrophil count decreased	No. of Events (%)	34 (11.5)	56 (19.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.493 (0.320, 0.759)
	Treatment P-value [b]		0.00117
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Platelet count decreased	No. of Events (%)	9 (3.0)	8 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.046 (0.402, 2.720)
	Treatment P-value [b]		0.92647
	Homogeneity P-value [c]		NA
Weight decreased	No. of Events (%)	48 (16.2)	21 (7.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.261 (1.350, 3.786)
	Treatment P-value [b]		0.00145
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
White blood cell count decreased	No. of Events (%)	16 (5.4)	34 (11.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.406 (0.223, 0.739)
	Treatment P-value [b]		0.00249
	Homogeneity P-value [c]		NA
Metabolism and nutrition disorders	No. of Events (%)	176 (59.5)	131 (45.0)
	Median Survival Est. (95% CI)	2.17 (1.41, 4.11)	25.33 (5.68, NC)
	Hazard Ratio (95% CI) [a]		1.400 (1.115, 1.758)
	Treatment P-value [b]		0.00353
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Decreased appetite	No. of Events (%)	123 (41.6)	82 (28.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.480 (1.118, 1.960)
	Treatment P-value [b]		0.00558
	Homogeneity P-value [c]		NA
Dehydration	No. of Events (%)	11 (3.7)	8 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.319 (0.530, 3.284)
	Treatment P-value [b]		0.55061
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
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
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

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
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]		0.694 (0.292, 1.650)
	Treatment P-value [b]		0.40555
	Homogeneity P-value [c]		NA
Hypoalbuminaemia	No. of Events (%)	14 (4.7)	11 (3.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.248 (0.566, 2.751)
	Treatment P-value [b]		0.57984
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Hypocalcaemia	No. of Events (%)	10 (3.4)	11 (3.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.771 (0.324, 1.837)
	Treatment P-value [b]		0.55575
	Homogeneity P-value [c]		NA
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]		1.880 (0.874, 4.046)
	Treatment P-value [b]		0.10049
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Hypomagnesaemia	No. of Events (%)	18 (6.1)	10 (3.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.780 (0.820, 3.863)
	Treatment P-value [b]		0.14123
	Homogeneity P-value [c]		NA
Hyponatraemia	No. of Events (%)	19 (6.4)	14 (4.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.282 (0.638, 2.577)
	Treatment P-value [b]		0.48507
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Hypophosphataemia	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]		1.080 (0.476, 2.451)
	Treatment P-value [b]		0.85472
	Homogeneity P-value [c]		NA
Musculoskeletal and connective tissue disorders	No. of Events (%)	106 (35.8)	123 (42.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	28.32 (14.85, NC)
	Hazard Ratio (95% CI) [a]		0.710 (0.546, 0.924)
	Treatment P-value [b]		0.01093
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Arthralgia	No. of Events (%)	29 (9.8)	41 (14.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.608 (0.376, 0.983)
	Treatment P-value [b]		0.04074
	Homogeneity P-value [c]		NA
Back pain	No. of Events (%)	31 (10.5)	27 (9.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.077 (0.640, 1.812)
	Treatment P-value [b]		0.77930
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Bone 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]		0.690 (0.256, 1.858)
	Treatment P-value [b]		0.46538
	Homogeneity P-value [c]		NA
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

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Groin pain	No. of Events (%)	6 (2.0)	5 (1.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.146 (0.348, 3.777)
	Treatment P-value [b]		0.82297
	Homogeneity P-value [c]		NA
Muscle spasms	No. of Events (%)	11 (3.7)	8 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.287 (0.517, 3.204)
	Treatment P-value [b]		0.58720
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
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]		2.069 (0.845, 5.067)
	Treatment P-value [b]		0.10402
	Homogeneity P-value [c]		NA
Myalgia	No. of Events (%)	15 (5.1)	35 (12.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.400 (0.218, 0.733)
	Treatment P-value [b]		0.00215
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Pain in extremity	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]		1.139 (0.589, 2.203)
	Treatment P-value [b]		0.69991
	Homogeneity P-value [c]		NA
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	No. of Events (%)	24 (8.1)	26 (8.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.869 (0.497, 1.517)
	Treatment P-value [b]		0.62029
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Malignant neoplasm progression	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]		1.198 (0.516, 2.782)
	Treatment P-value [b]		0.67458
	Homogeneity P-value [c]		NA
Nervous system disorders	No. of Events (%)	192 (64.9)	139 (47.8)
	Median Survival Est. (95% CI)	2.83 (2.20, 3.68)	6.93 (3.94, NC)
	Hazard Ratio (95% CI) [a]		1.426 (1.144, 1.778)
	Treatment P-value [b]		0.00148
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Dizziness	No. of Events (%)	27 (9.1)	16 (5.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.531 (0.822, 2.852)
	Treatment P-value [b]		0.17592
	Homogeneity P-value [c]		NA
Dysgeusia	No. of Events (%)	75 (25.3)	24 (8.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.281 (2.067, 5.207)
	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.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Headache	No. of Events (%)	13 (4.4)	17 (5.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.726 (0.351, 1.500)
	Treatment P-value [b]		0.38488
	Homogeneity P-value [c]		NA
Neuropathy peripheral	No. of Events (%)	21 (7.1)	17 (5.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.149 (0.605, 2.183)
	Treatment P-value [b]		0.67044
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Paraesthesia	No. of Events (%)	16 (5.4)	10 (3.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.532 (0.692, 3.393)
	Treatment P-value [b]		0.28910
	Homogeneity P-value [c]		NA
Peripheral motor neuropathy	No. of Events (%)	13 (4.4)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00102
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Peripheral sensorimotor neuropathy	No. of Events (%)	9 (3.0)	2 (0.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.144 (0.894, 19.204)
	Treatment P-value [b]		0.04853
	Homogeneity P-value [c]		NA
Peripheral sensory neuropathy	No. of Events (%)	105 (35.5)	68 (23.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.421 (1.046, 1.931)
	Treatment P-value [b]		0.02328
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Polyneuropathy	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]		0.967 (0.311, 3.006)
	Treatment P-value [b]		0.95405
	Homogeneity P-value [c]		NA
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

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Psychiatric disorders	No. of Events (%)	57 (19.3)	49 (16.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.078 (0.734, 1.582)
	Treatment P-value [b]		0.70616
	Homogeneity P-value [c]		NA
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]		1.225 (0.424, 3.541)
	Treatment P-value [b]		0.70690
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
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
Depression	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]		5.149 (1.139, 23.272)
	Treatment P-value [b]		0.01762
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Insomnia	No. of Events (%)	35 (11.8)	25 (8.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.295 (0.773, 2.170)
	Treatment P-value [b]		0.32397
	Homogeneity P-value [c]		NA
Renal and urinary disorders	No. of Events (%)	84 (28.4)	57 (19.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.458 (1.040, 2.045)
	Treatment P-value [b]		0.02759
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Acute kidney injury	No. of Events (%)	20 (6.8)	9 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.168 (0.986, 4.766)
	Treatment P-value [b]		0.04828
	Homogeneity P-value [c]		NA
Dysuria	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]		2.017 (0.694, 5.864)
	Treatment P-value [b]		0.18866
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Haematuria	No. of Events (%)	41 (13.9)	26 (8.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.463 (0.892, 2.399)
	Treatment P-value [b]		0.12890
	Homogeneity P-value [c]		NA
Pollakiuria	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]		3.416 (0.716, 16.303)
	Treatment P-value [b]		0.10175
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Urinary incontinence	No. of Events (%)	5 (1.7)	7 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.671 (0.212, 2.119)
	Treatment P-value [b]		0.49322
	Homogeneity P-value [c]		NA
Urinary retention	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]		0.779 (0.237, 2.563)
	Treatment P-value [b]		0.68007
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Reproductive system and breast disorders	No. of Events (%)	11 (3.7)	12 (4.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.848 (0.374, 1.925)
	Treatment P-value [b]		0.69313
	Homogeneity P-value [c]		NA
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	102 (34.5)	74 (25.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.381 (1.022, 1.865)
	Treatment P-value [b]		0.03480
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Cough	No. of Events (%)	25 (8.4)	19 (6.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.149 (0.629, 2.097)
	Treatment P-value [b]		0.65092
	Homogeneity P-value [c]		NA
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]		3.475 (0.731, 16.529)
	Treatment P-value [b]		0.09588
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Dyspnoea	No. of Events (%)	29 (9.8)	30 (10.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.897 (0.538, 1.497)
	Treatment P-value [b]		0.67792
	Homogeneity P-value [c]		NA
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

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Epistaxis	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]		2.596 (0.825, 8.169)
	Treatment P-value [b]		0.09059
	Homogeneity P-value [c]		NA
Nasal congestion	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]		2.260 (0.582, 8.778)
	Treatment P-value [b]		0.22620
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Oropharyngeal pain	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]		2.910 (0.784, 10.793)
	Treatment P-value [b]		0.09453
	Homogeneity P-value [c]		NA
Productive cough	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]		1.621 (0.473, 5.560)
	Treatment P-value [b]		0.43779
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Pulmonary embolism	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]		2.415 (0.638, 9.142)
	Treatment P-value [b]		0.18040
	Homogeneity P-value [c]		NA
Rhinorrhoea	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]		1.441 (0.627, 3.313)
	Treatment P-value [b]		0.38736
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Skin and subcutaneous tissue disorders	No. of Events (%)	238 (80.4)	155 (53.3)
	Median Survival Est. (95% CI)	0.62 (0.49, 0.79)	2.86 (1.41, 12.22)
	Hazard Ratio (95% CI) [a]		2.158 (1.755, 2.653)
	Treatment P-value [b]		<.00001
	Homogeneity P-value [c]		NA
Alopecia	No. of Events (%)	141 (47.6)	113 (38.8)
	Median Survival Est. (95% CI)	12.42 (2.40, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.087 (0.847, 1.394)
	Treatment P-value [b]		0.49959
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
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]		8.893 (1.126, 70.208)
	Treatment P-value [b]		0.01206
	Homogeneity P-value [c]		NA
Drug eruption	No. of Events (%)	26 (8.8)	6 (2.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.690 (1.922, 11.444)
	Treatment P-value [b]		0.00019
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Dry skin	No. of Events (%)	53 (17.9)	13 (4.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.271 (2.319, 7.867)
	Treatment P-value [b]		<.00001
	Homogeneity P-value [c]		NA
Erythema	No. of Events (%)	13 (4.4)	5 (1.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.525 (0.900, 7.086)
	Treatment P-value [b]		0.06837
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Pruritus	No. of Events (%)	103 (34.8)	22 (7.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.820 (3.663, 9.248)
	Treatment P-value [b]		<.00001
	Homogeneity P-value [c]		NA
Rash	No. of Events (%)	52 (17.6)	21 (7.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.546 (1.532, 4.231)
	Treatment P-value [b]		0.00019
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
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]		9.685 (1.238, 75.764)
	Treatment P-value [b]		0.00792
	Homogeneity P-value [c]		NA
Rash maculo-papular	No. of Events (%)	52 (17.6)	8 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.210 (3.410, 15.246)
	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.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Skin hyperpigmentation	No. of Events (%)	20 (6.8)	2 (0.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		10.886 (2.535, 46.745)
	Treatment P-value [b]		0.00006
	Homogeneity P-value [c]		NA
Vascular disorders	No. of Events (%)	48 (16.2)	44 (15.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.998 (0.661, 1.505)
	Treatment P-value [b]		0.98795
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Hypertension	No. of Events (%)	13 (4.4)	14 (4.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.780 (0.362, 1.677)
	Treatment P-value [b]		0.52321
	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]		1.619 (0.670, 3.910)
	Treatment P-value [b]		0.28223
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		1.009 (0.768, 1.326)
	Treatment P-value [b]		0.85297
	Interaction P-value [c]		0.40732
Blood and lymphatic system disorders	No. of Events (%)	29 (27.4)	37 (35.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.642 (0.395, 1.044)
	Treatment P-value [b]		0.07607
	Interaction P-value [c]		0.51028

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Anaemia	No. of Events (%)	23 (21.7)	29 (28.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.678 (0.392, 1.172)
	Treatment P-value [b]		0.17172
	Interaction P-value [c]		0.60768
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

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Eye disorders	No. of Events (%)	27 (25.5)	7 (6.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.897 (1.697, 8.947)
	Treatment P-value [b]		0.00054
	Interaction P-value [c]		0.81771
Dry eye	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]		3.754 (0.797, 17.682)
	Treatment P-value [b]		0.07047
	Interaction P-value [c]		0.37187

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Lacrimation increased	No. of Events (%)	13 (12.3)	2 (1.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.200 (1.399, 27.475)
	Treatment P-value [b]		0.00653
	Interaction P-value [c]		0.19782
Vision blurred	No. of Events (%)	3 (2.8)	3 (2.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.897 (0.181, 4.443)
	Treatment P-value [b]		0.88024
	Interaction P-value [c]		0.06484

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Diarrhoea	No. of Events (%)	34 (32.1)	23 (22.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.432 (0.844, 2.432)
	Treatment P-value [b]		0.19335
	Interaction P-value [c]		0.78451
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]		0.98594

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Chills	No. of Events (%)	6 (5.7)	1 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.657 (0.681, 47.004)
	Treatment P-value [b]		0.07412
	Interaction P-value [c]		0.55328
Fatigue	No. of Events (%)	35 (33.0)	23 (22.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.458 (0.861, 2.467)
	Treatment P-value [b]		0.16011
	Interaction P-value [c]		0.71419

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Pyrexia	No. of Events (%)	26 (24.5)	16 (15.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.585 (0.850, 2.955)
	Treatment P-value [b]		0.13320
	Interaction P-value [c]		0.80489
Infections and infestations	No. of Events (%)	51 (48.1)	33 (32.0)
	Median Survival Est. (95% CI)	11.33 (3.25, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.548 (0.999, 2.399)
	Treatment P-value [b]		0.04774
	Interaction P-value [c]		0.85104

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		0.18147
	Interaction P-value [c]		0.99141
Alanine aminotransferase increased	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]		3.910 (0.830, 18.411)
	Treatment P-value [b]		0.06239
	Interaction P-value [c]		0.97650

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Aspartate aminotransferase increased	No. of Events (%)	11 (10.4)	3 (2.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.605 (1.006, 12.924)
	Treatment P-value [b]		0.03421
	Interaction P-value [c]		0.32975
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]		4.189 (0.905, 19.399)
	Treatment P-value [b]		0.03830
	Interaction P-value [c]		0.75272

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		0.368 (0.151, 0.895)
	Treatment P-value [b]		0.02844
	Interaction P-value [c]		0.34503
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]		2.721 (1.073, 6.901)
	Treatment P-value [b]		0.02909
	Interaction P-value [c]		0.68400

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		0.235 (0.065, 0.842)
	Treatment P-value [b]		0.01992
	Interaction P-value [c]		0.27843
Metabolism and nutrition disorders	No. of Events (%)	61 (57.5)	42 (40.8)
	Median Survival Est. (95% CI)	3.25 (1.58, NC)	NC (6.05, NC)
	Hazard Ratio (95% CI) [a]		1.496 (1.010, 2.216)
	Treatment P-value [b]		0.04104
	Interaction P-value [c]		0.67123

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Decreased appetite	No. of Events (%)	44 (41.5)	27 (26.2)
	Median Survival Est. (95% CI)	NC (5.55, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.589 (0.984, 2.566)
	Treatment P-value [b]		0.05501
	Interaction P-value [c]		0.78178
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

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Musculoskeletal and connective tissue disorders	No. of Events (%)	37 (34.9)	48 (46.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	6.01 (2.56, NC)
	Hazard Ratio (95% CI) [a]		0.596 (0.388, 0.915)
	Treatment P-value [b]		0.01539
	Interaction P-value [c]		0.27228
Arthralgia	No. of Events (%)	12 (11.3)	16 (15.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.659 (0.312, 1.394)
	Treatment P-value [b]		0.26744
	Interaction P-value [c]		0.87895

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Myalgia	No. of Events (%)	6 (5.7)	14 (13.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.379 (0.145, 0.986)
	Treatment P-value [b]		0.03502
	Interaction P-value [c]		0.94407
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]		1.467 (1.011, 2.128)
	Treatment P-value [b]		0.03961
	Interaction P-value [c]		0.98635

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Dysgeusia	No. of Events (%)	27 (25.5)	10 (9.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.761 (1.336, 5.703)
	Treatment P-value [b]		0.00428
	Interaction P-value [c]		0.53568
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]		1.040 (0.626, 1.730)
	Treatment P-value [b]		0.87731
	Interaction P-value [c]		0.10672

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Renal and urinary disorders	No. of Events (%)	31 (29.2)	23 (22.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.329 (0.775, 2.280)
	Treatment P-value [b]		0.28593
	Interaction P-value [c]		0.66716
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	30 (28.3)	22 (21.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.327 (0.766, 2.301)
	Treatment P-value [b]		0.31561
	Interaction P-value [c]		0.82853

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Skin and subcutaneous tissue disorders	No. of Events (%)	89 (84.0)	53 (51.5)
	Median Survival Est. (95% CI)	0.62 (0.46, 0.89)	3.12 (0.72, NC)
	Hazard Ratio (95% CI) [a]		2.346 (1.668, 3.300)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.40541
Drug eruption	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]		3.427 (0.712, 16.498)
	Treatment P-value [b]		0.10677
	Interaction P-value [c]		0.73593

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Dry skin	No. of Events (%)	20 (18.9)	6 (5.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.310 (1.329, 8.244)
	Treatment P-value [b]		0.00609
	Interaction P-value [c]		0.53044
Pruritus	No. of Events (%)	39 (36.8)	6 (5.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.613 (3.223, 17.986)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.36445

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Rash	No. of Events (%)	20 (18.9)	9 (8.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.200 (1.002, 4.834)
	Treatment P-value [b]		0.04542
	Interaction P-value [c]		0.67627
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]		9.724 (2.265, 41.747)
	Treatment P-value [b]		0.00016
	Interaction P-value [c]		0.54512

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Skin hyperpigmentation	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]		0.00999
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		0.874 (0.713, 1.072)
	Treatment P-value [b]		0.17707
	Interaction P-value [c]		0.40732
Blood and lymphatic system disorders	No. of Events (%)	58 (30.5)	91 (48.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	7.85 (4.07, NC)
	Hazard Ratio (95% CI) [a]		0.527 (0.379, 0.733)
	Treatment P-value [b]		0.00011
	Interaction P-value [c]		0.51028

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Anaemia	No. of Events (%)	39 (20.5)	62 (33.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.567 (0.380, 0.847)
	Treatment P-value [b]		0.00501
	Interaction P-value [c]		0.60768
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.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Eye disorders	No. of Events (%)	59 (31.1)	19 (10.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.473 (2.071, 5.825)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.81771
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]		12.059 (1.569, 92.696)
	Treatment P-value [b]		0.00226
	Interaction P-value [c]		0.37187

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Lacrimation increased	No. of Events (%)	21 (11.1)	10 (5.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.072 (0.975, 4.400)
	Treatment P-value [b]		0.05166
	Interaction P-value [c]		0.19782
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]		6.996 (1.590, 30.784)
	Treatment P-value [b]		0.00257
	Interaction P-value [c]		0.06484

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Diarrhoea	No. of Events (%)	72 (37.9)	47 (25.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.567 (1.085, 2.264)
	Treatment P-value [b]		0.01544
	Interaction P-value [c]		0.78451
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]		2.168 (0.884, 5.318)
	Treatment P-value [b]		0.08472
	Interaction P-value [c]		0.98594

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Chills	No. of Events (%)	14 (7.4)	5 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.779 (1.001, 7.716)
	Treatment P-value [b]		0.03955
	Interaction P-value [c]		0.55328
Fatigue	No. of Events (%)	75 (39.5)	58 (30.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.296 (0.920, 1.827)
	Treatment P-value [b]		0.13429
	Interaction P-value [c]		0.71419

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Pyrexia	No. of Events (%)	42 (22.1)	29 (15.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (29.73, NC)
	Hazard Ratio (95% CI) [a]		1.436 (0.895, 2.306)
	Treatment P-value [b]		0.13806
	Interaction P-value [c]		0.80489
Infections and infestations	No. of Events (%)	106 (55.8)	78 (41.5)
	Median Survival Est. (95% CI)	3.84 (2.86, 8.64)	NC (9.20, NC)
	Hazard Ratio (95% CI) [a]		1.472 (1.098, 1.972)
	Treatment P-value [b]		0.00916
	Interaction P-value [c]		0.85104

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Conjunctivitis	No. of Events (%)	17 (8.9)	3 (1.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.669 (1.661, 19.352)
	Treatment P-value [b]		0.00174
	Interaction P-value [c]		0.99141
Alanine aminotransferase increased	No. of Events (%)	19 (10.0)	5 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.803 (1.420, 10.191)
	Treatment P-value [b]		0.00405
	Interaction P-value [c]		0.97650

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		8.610 (2.599, 28.519)
	Treatment P-value [b]		0.00002
	Interaction P-value [c]		0.32975
Blood creatinine increased	No. of Events (%)	19 (10.0)	6 (3.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (30.62, NC)
	Hazard Ratio (95% CI) [a]		3.144 (1.255, 7.875)
	Treatment P-value [b]		0.01064
	Interaction P-value [c]		0.75272

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Neutrophil count decreased	No. of Events (%)	27 (14.2)	40 (21.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.600 (0.368, 0.978)
	Treatment P-value [b]		0.03530
	Interaction P-value [c]		0.34503
Weight decreased	No. of Events (%)	31 (16.3)	15 (8.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.158 (1.165, 3.998)
	Treatment P-value [b]		0.01229
	Interaction P-value [c]		0.68400

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
White blood cell count decreased	No. of Events (%)	13 (6.8)	23 (12.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.522 (0.265, 1.032)
	Treatment P-value [b]		0.05491
	Interaction P-value [c]		0.27843
Metabolism and nutrition disorders	No. of Events (%)	115 (60.5)	89 (47.3)
	Median Survival Est. (95% CI)	1.91 (1.05, 4.86)	16.59 (2.79, NC)
	Hazard Ratio (95% CI) [a]		1.348 (1.022, 1.779)
	Treatment P-value [b]		0.03685
	Interaction P-value [c]		0.67123

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Decreased appetite	No. of Events (%)	79 (41.6)	55 (29.3)
	Median Survival Est. (95% CI)	NC (9.10, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.462 (1.036, 2.064)
	Treatment P-value [b]		0.03009
	Interaction P-value [c]		0.78178
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

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Musculoskeletal and connective tissue disorders	No. of Events (%)	69 (36.3)	75 (39.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	28.32 (14.85, NC)
	Hazard Ratio (95% CI) [a]		0.806 (0.581, 1.118)
	Treatment P-value [b]		0.19630
	Interaction P-value [c]		0.27228
Arthralgia	No. of Events (%)	17 (8.9)	25 (13.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.611 (0.330, 1.132)
	Treatment P-value [b]		0.11624
	Interaction P-value [c]		0.87895

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Myalgia	No. of Events (%)	9 (4.7)	21 (11.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.396 (0.181, 0.864)
	Treatment P-value [b]		0.01734
	Interaction P-value [c]		0.94407
Nervous system disorders	No. of Events (%)	124 (65.3)	92 (48.9)
	Median Survival Est. (95% CI)	2.79 (1.87, 3.81)	6.67 (2.79, NC)
	Hazard Ratio (95% CI) [a]		1.461 (1.115, 1.914)
	Treatment P-value [b]		0.00623
	Interaction P-value [c]		0.98635

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Dysgeusia	No. of Events (%)	48 (25.3)	14 (7.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.714 (2.047, 6.736)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.53568
Peripheral sensory neuropathy	No. of Events (%)	72 (37.9)	41 (21.8)
	Median Survival Est. (95% CI)	NC (6.60, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.758 (1.198, 2.580)
	Treatment P-value [b]		0.00352
	Interaction P-value [c]		0.10672

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Renal and urinary disorders	No. of Events (%)	53 (27.9)	34 (18.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.547 (1.005, 2.380)
	Treatment P-value [b]		0.04914
	Interaction P-value [c]		0.66716
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	72 (37.9)	52 (27.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.427 (0.999, 2.039)
	Treatment P-value [b]		0.04773
	Interaction P-value [c]		0.82853

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Skin and subcutaneous tissue disorders	No. of Events (%)	149 (78.4)	102 (54.3)
	Median Survival Est. (95% CI)	0.62 (0.43, 0.89)	2.86 (0.76, 12.22)
	Hazard Ratio (95% CI) [a]		1.960 (1.522, 2.524)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.40541
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]		4.757 (1.618, 13.987)
	Treatment P-value [b]		0.00155
	Interaction P-value [c]		0.73593

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Dry skin	No. of Events (%)	33 (17.4)	7 (3.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.897 (2.166, 11.071)
	Treatment P-value [b]		0.00002
	Interaction P-value [c]		0.53044
Pruritus	No. of Events (%)	64 (33.7)	16 (8.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.751 (2.746, 8.219)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.36445

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Rash	No. of Events (%)	32 (16.8)	12 (6.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.740 (1.411, 5.321)
	Treatment P-value [b]		0.00176
	Interaction P-value [c]		0.67627
Rash maculo-papular	No. of Events (%)	33 (17.4)	6 (3.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.758 (2.412, 13.747)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.54512

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Skin hyperpigmentation	No. of Events (%)	13 (6.8)	2 (1.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.550 (1.477, 29.045)
	Treatment P-value [b]		0.00438
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Any Event	No. of Events (%)	241 (98.4)	224 (99.1)
	Median Survival Est. (95% CI)	0.20 (0.13, 0.23)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.922 (0.768, 1.106)
	Treatment P-value [b]		0.37834
	Interaction P-value [c]		0.93354
Blood and lymphatic system disorders	No. of Events (%)	71 (29.0)	95 (42.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (5.98, NC)
	Hazard Ratio (95% CI) [a]		0.577 (0.424, 0.785)
	Treatment P-value [b]		0.00038
	Interaction P-value [c]		0.78519

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Anaemia	No. of Events (%)	52 (21.2)	69 (30.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.619 (0.432, 0.888)
	Treatment P-value [b]		0.00776
	Interaction P-value [c]		0.76852
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.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	67 (27.3)	18 (8.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.655 (2.172, 6.150)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.92778
Dry eye	No. of Events (%)	13 (5.3)	3 (1.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.883 (1.106, 13.628)
	Treatment P-value [b]		0.02247
	Interaction P-value [c]		0.98904

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Lacrimation increased	No. of Events (%)	30 (12.2)	7 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.886 (1.707, 8.848)
	Treatment P-value [b]		0.00052
	Interaction P-value [c]		0.09599
Vision blurred	No. of Events (%)	10 (4.1)	4 (1.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.185 (0.685, 6.969)
	Treatment P-value [b]		0.17916
	Interaction P-value [c]		0.21529

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Diarrhoea	No. of Events (%)	85 (34.7)	50 (22.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.579 (1.113, 2.240)
	Treatment P-value [b]		0.00969
	Interaction P-value [c]		0.79654
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]		3.729 (1.400, 9.937)
	Treatment P-value [b]		0.00470
	Interaction P-value [c]		0.74203

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Chills	No. of Events (%)	17 (6.9)	4 (1.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.858 (1.298, 11.469)
	Treatment P-value [b]		0.00912
	Interaction P-value [c]		0.52386
Fatigue	No. of Events (%)	86 (35.1)	62 (27.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.256 (0.906, 1.742)
	Treatment P-value [b]		0.17053
	Interaction P-value [c]		0.32630

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Pyrexia	No. of Events (%)	59 (24.1)	35 (15.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.560 (1.027, 2.370)
	Treatment P-value [b]		0.03375
	Interaction P-value [c]		0.53553
Infections and infestations	No. of Events (%)	128 (52.2)	80 (35.4)
	Median Survival Est. (95% CI)	6.60 (3.55, 21.19)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.563 (1.182, 2.066)
	Treatment P-value [b]		0.00155
	Interaction P-value [c]		0.64791

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		12.537 (1.649, 95.325)
	Treatment P-value [b]		0.00164
	Interaction P-value [c]		0.32492
Alanine aminotransferase increased	No. of Events (%)	22 (9.0)	5 (2.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.035 (1.528, 10.657)
	Treatment P-value [b]		0.00214
	Interaction P-value [c]		0.86053

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Aspartate aminotransferase increased	No. of Events (%)	31 (12.7)	6 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.858 (2.027, 11.646)
	Treatment P-value [b]		0.00009
	Interaction P-value [c]		0.98801
Blood creatinine increased	No. of Events (%)	25 (10.2)	5 (2.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.497 (1.720, 11.755)
	Treatment P-value [b]		0.00074
	Interaction P-value [c]		0.18753

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Neutrophil count decreased	No. of Events (%)	31 (12.7)	40 (17.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.631 (0.395, 1.009)
	Treatment P-value [b]		0.05453
	Interaction P-value [c]		0.10859
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]		2.556 (1.355, 4.819)
	Treatment P-value [b]		0.00255
	Interaction P-value [c]		0.81431

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
White blood cell count decreased	No. of Events (%)	14 (5.7)	25 (11.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.468 (0.243, 0.901)
	Treatment P-value [b]		0.02213
	Interaction P-value [c]		0.51958
Metabolism and nutrition disorders	No. of Events (%)	141 (57.6)	96 (42.5)
	Median Survival Est. (95% CI)	2.99 (1.77, 6.34)	NC (7.23, NC)
	Hazard Ratio (95% CI) [a]		1.395 (1.076, 1.809)
	Treatment P-value [b]		0.01061
	Interaction P-value [c]		0.69378

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Decreased appetite	No. of Events (%)	102 (41.6)	56 (24.8)
	Median Survival Est. (95% CI)	NC (9.13, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.718 (1.240, 2.380)
	Treatment P-value [b]		0.00098
	Interaction P-value [c]		0.14414
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.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Musculoskeletal and connective tissue disorders	No. of Events (%)	86 (35.1)	96 (42.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (5.09, NC)
	Hazard Ratio (95% CI) [a]		0.686 (0.512, 0.918)
	Treatment P-value [b]		0.01205
	Interaction P-value [c]		0.41909
Arthralgia	No. of Events (%)	24 (9.8)	31 (13.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.646 (0.379, 1.101)
	Treatment P-value [b]		0.10577
	Interaction P-value [c]		0.86948

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Myalgia	No. of Events (%)	13 (5.3)	26 (11.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.424 (0.218, 0.826)
	Treatment P-value [b]		0.00946
	Interaction P-value [c]		0.59183
Nervous system disorders	No. of Events (%)	160 (65.3)	104 (46.0)
	Median Survival Est. (95% CI)	2.99 (2.20, 3.71)	6.93 (4.17, NC)
	Hazard Ratio (95% CI) [a]		1.525 (1.191, 1.952)
	Treatment P-value [b]		0.00055
	Interaction P-value [c]		0.54166

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Dysgeusia	No. of Events (%)	63 (25.7)	18 (8.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.435 (2.034, 5.801)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.77562
Peripheral motor neuropathy	No. of Events (%)	12 (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]		0.00200
	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.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	88 (35.9)	55 (24.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.378 (0.984, 1.930)
	Treatment P-value [b]		0.05870
	Interaction P-value [c]		0.55179
Depression	No. of Events (%)	11 (4.5)	2 (0.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.834 (1.071, 21.822)
	Treatment P-value [b]		0.02335
	Interaction P-value [c]		0.99954

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Renal and urinary disorders	No. of Events (%)	73 (29.8)	46 (20.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.446 (1.000, 2.092)
	Treatment P-value [b]		0.04733
	Interaction P-value [c]		0.90596
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	83 (33.9)	64 (28.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.177 (0.850, 1.631)
	Treatment P-value [b]		0.32936
	Interaction P-value [c]		0.03293

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Skin and subcutaneous tissue disorders	No. of Events (%)	198 (80.8)	118 (52.2)
	Median Survival Est. (95% CI)	0.66 (0.46, 0.82)	3.02 (1.31, NC)
	Hazard Ratio (95% CI) [a]		2.135 (1.697, 2.685)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.69176
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]		7.892 (1.000, 62.308)
	Treatment P-value [b]		0.01999
	Interaction P-value [c]		0.99949

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Drug eruption	No. of Events (%)	25 (10.2)	5 (2.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.674 (1.789, 12.211)
	Treatment P-value [b]		0.00053
	Interaction P-value [c]		0.38118
Dry skin	No. of Events (%)	43 (17.6)	10 (4.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.021 (2.020, 8.003)
	Treatment P-value [b]		0.00002
	Interaction P-value [c]		0.78894

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Pruritus	No. of Events (%)	83 (33.9)	18 (8.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.994 (2.999, 8.316)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.37900
Rash	No. of Events (%)	48 (19.6)	17 (7.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.698 (1.551, 4.692)
	Treatment P-value [b]		0.00025
	Interaction P-value [c]		0.32285

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Rash maculo-papular	No. of Events (%)	44 (18.0)	5 (2.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		8.494 (3.368, 21.422)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.31974
Skin hyperpigmentation	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]		13.709 (1.811, 103.780)
	Treatment P-value [b]		0.00083
	Interaction P-value [c]		0.64535

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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=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]		0.906 (0.624, 1.314)
	Treatment P-value [b]		0.64142
	Interaction P-value [c]		0.93354
Blood and lymphatic system disorders	No. of Events (%)	16 (31.4)	33 (50.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	12.94 (1.41, NC)
	Hazard Ratio (95% CI) [a]		0.526 (0.289, 0.956)
	Treatment P-value [b]		0.03301
	Interaction P-value [c]		0.78519

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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=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]		0.547 (0.259, 1.155)
	Treatment P-value [b]		0.11719
	Interaction P-value [c]		0.76852
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.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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=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]		3.824 (1.673, 8.738)
	Treatment P-value [b]		0.00091
	Interaction P-value [c]		0.92778
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]		0.00211
	Interaction P-value [c]		0.98904

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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=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]		1.041 (0.279, 3.877)
	Treatment P-value [b]		0.91920
	Interaction P-value [c]		0.09599
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]		9.933 (1.222, 80.751)
	Treatment P-value [b]		0.00795
	Interaction P-value [c]		0.21529

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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=51)	Chemotherapy (N=65)
Diarrhoea	No. of Events (%)	21 (41.2)	20 (30.8)
	Median Survival Est. (95% CI)	NC (1.74, NC)	NC (14.98, NC)
	Hazard Ratio (95% CI) [a]		1.439 (0.780, 2.656)
	Treatment P-value [b]		0.25033
	Interaction P-value [c]		0.79654
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]		2.683 (0.491, 14.651)
	Treatment P-value [b]		0.22172
	Interaction P-value [c]		0.74203

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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=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]		1.952 (0.326, 11.686)
	Treatment P-value [b]		0.45686
	Interaction P-value [c]		0.52386
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]		1.771 (0.970, 3.233)
	Treatment P-value [b]		0.04767
	Interaction P-value [c]		0.32630

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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=51)	Chemotherapy (N=65)
Pyrexia	No. of Events (%)	9 (17.6)	10 (15.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	29.73 (29.73, NC)
	Hazard Ratio (95% CI) [a]		1.140 (0.463, 2.805)
	Treatment P-value [b]		0.86077
	Interaction P-value [c]		0.53553
Infections and infestations	No. of Events (%)	29 (56.9)	31 (47.7)
	Median Survival Est. (95% CI)	2.56 (1.84, NC)	17.68 (3.29, NC)
	Hazard Ratio (95% CI) [a]		1.366 (0.823, 2.267)
	Treatment P-value [b]		0.23758
	Interaction P-value [c]		0.64791

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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=51)	Chemotherapy (N=65)
Conjunctivitis	No. of Events (%)	5 (9.8)	2 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.382 (0.656, 17.441)
	Treatment P-value [b]		0.13210
	Interaction P-value [c]		0.32492
Alanine aminotransferase increased	No. of Events (%)	5 (9.8)	2 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (25.56, NC)
	Hazard Ratio (95% CI) [a]		3.401 (0.660, 17.535)
	Treatment P-value [b]		0.13396
	Interaction P-value [c]		0.86053

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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=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]		0.98801
Blood creatinine increased	No. of Events (%)	3 (5.9)	3 (4.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	30.62 (30.62, NC)
	Hazard Ratio (95% CI) [a]		1.282 (0.259, 6.357)
	Treatment P-value [b]		0.76641
	Interaction P-value [c]		0.18753

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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=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]		0.214 (0.062, 0.735)
	Treatment P-value [b]		0.00792
	Interaction P-value [c]		0.10859
Weight decreased	No. of Events (%)	12 (23.5)	8 (12.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (25.56, NC)
	Hazard Ratio (95% CI) [a]		2.241 (0.916, 5.484)
	Treatment P-value [b]		0.06947
	Interaction P-value [c]		0.81431

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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=51)	Chemotherapy (N=65)
White blood cell count decreased	No. of Events (%)	2 (3.9)	9 (13.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.271 (0.058, 1.253)
	Treatment P-value [b]		0.07165
	Interaction P-value [c]		0.51958
Metabolism and nutrition disorders	No. of Events (%)	35 (68.6)	35 (53.8)
	Median Survival Est. (95% CI)	0.69 (0.46, 4.11)	5.29 (1.45, NC)
	Hazard Ratio (95% CI) [a]		1.554 (0.972, 2.483)
	Treatment P-value [b]		0.07897
	Interaction P-value [c]		0.69378

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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=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]		1.049 (0.590, 1.865)
	Treatment P-value [b]		0.83503
	Interaction P-value [c]		0.14414
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

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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=51)	Chemotherapy (N=65)
Musculoskeletal and connective tissue disorders	No. of Events (%)	20 (39.2)	27 (41.5)
	Median Survival Est. (95% CI)	NC (3.42, NC)	28.32 (4.27, NC)
	Hazard Ratio (95% CI) [a]		0.896 (0.502, 1.597)
	Treatment P-value [b]		0.63322
	Interaction P-value [c]		0.41909
Arthralgia	No. of Events (%)	5 (9.8)	10 (15.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.584 (0.200, 1.709)
	Treatment P-value [b]		0.32468
	Interaction P-value [c]		0.86948

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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=51)	Chemotherapy (N=65)
Myalgia	No. of Events (%)	2 (3.9)	9 (13.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.269 (0.058, 1.243)
	Treatment P-value [b]		0.06813
	Interaction P-value [c]		0.59183
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]		1.289 (0.798, 2.082)
	Treatment P-value [b]		0.39080
	Interaction P-value [c]		0.54166

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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=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]		2.923 (1.097, 7.789)
	Treatment P-value [b]		0.03073
	Interaction P-value [c]		0.77562
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]		0.99981

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.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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=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]		1.756 (0.853, 3.615)
	Treatment P-value [b]		0.13282
	Interaction P-value [c]		0.55179
Depression	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]		0.99954

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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=51)	Chemotherapy (N=65)
Renal and urinary disorders	No. of Events (%)	11 (21.6)	11 (16.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (25.26, NC)
	Hazard Ratio (95% CI) [a]		1.369 (0.593, 3.159)
	Treatment P-value [b]		0.51056
	Interaction P-value [c]		0.90596
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	19 (37.3)	10 (15.4)
	Median Survival Est. (95% CI)	NC (3.94, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.913 (1.354, 6.265)
	Treatment P-value [b]		0.00556
	Interaction P-value [c]		0.03293

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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=51)	Chemotherapy (N=65)
Skin and subcutaneous tissue disorders	No. of Events (%)	40 (78.4)	37 (56.9)
	Median Survival Est. (95% CI)	0.56 (0.30, 1.12)	2.86 (0.69, NC)
	Hazard Ratio (95% CI) [a]		1.929 (1.233, 3.018)
	Treatment P-value [b]		0.00517
	Interaction P-value [c]		0.69176
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

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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=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]		1.260 (0.079, 20.144)
	Treatment P-value [b]		0.86783
	Interaction P-value [c]		0.38118
Dry skin	No. of Events (%)	10 (19.6)	3 (4.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (26.94, NC)
	Hazard Ratio (95% CI) [a]		4.910 (1.351, 17.848)
	Treatment P-value [b]		0.00975
	Interaction P-value [c]		0.78894

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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=51)	Chemotherapy (N=65)
Pruritus	No. of Events (%)	20 (39.2)	4 (6.2)
	Median Survival Est. (95% CI)	NC (0.92, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		8.512 (2.910, 24.902)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.37900
Rash	No. of Events (%)	4 (7.8)	4 (6.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.271 (0.318, 5.083)
	Treatment P-value [b]		0.73206
	Interaction P-value [c]		0.32285

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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=51)	Chemotherapy (N=65)
Rash maculo-papular	No. of Events (%)	8 (15.7)	3 (4.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.736 (0.991, 14.089)
	Treatment P-value [b]		0.04652
	Interaction P-value [c]		0.31974
Skin hyperpigmentation	No. of Events (%)	5 (9.8)	1 (1.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (26.87, NC)
	Hazard Ratio (95% CI) [a]		6.856 (0.800, 58.734)
	Treatment P-value [b]		0.05257
	Interaction P-value [c]		0.64535

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
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]		0.979 (0.812, 1.180)
	Treatment P-value [b]		0.90929
	Interaction P-value [c]		0.16730
Blood and lymphatic system disorders	No. of Events (%)	62 (26.5)	100 (45.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	22.97 (4.76, NC)
	Hazard Ratio (95% CI) [a]		0.464 (0.338, 0.638)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.01534

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	42 (17.9)	65 (29.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.537 (0.364, 0.792)
	Treatment P-value [b]		0.00118
	Interaction P-value [c]		0.19653
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.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Eye disorders	No. of Events (%)	74 (31.6)	18 (8.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.234 (2.529, 7.087)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.12062
Dry eye	No. of Events (%)	16 (6.8)	2 (0.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.370 (1.694, 32.063)
	Treatment P-value [b]		0.00167
	Interaction P-value [c]		0.75482

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Lacrimation increased	No. of Events (%)	31 (13.2)	9 (4.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.156 (1.502, 6.630)
	Treatment P-value [b]		0.00131
	Interaction P-value [c]		0.27881
Vision blurred	No. of Events (%)	15 (6.4)	4 (1.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.367 (1.117, 10.148)
	Treatment P-value [b]		0.02242
	Interaction P-value [c]		0.80602

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Diarrhoea	No. of Events (%)	85 (36.3)	48 (21.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.688 (1.184, 2.405)
	Treatment P-value [b]		0.00289
	Interaction P-value [c]		0.27151
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]		3.020 (1.106, 8.244)
	Treatment P-value [b]		0.02145
	Interaction P-value [c]		0.60117

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Chills	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]		2.937 (1.075, 8.022)
	Treatment P-value [b]		0.02827
	Interaction P-value [c]		0.69649
Fatigue	No. of Events (%)	90 (38.5)	56 (25.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.515 (1.085, 2.115)
	Treatment P-value [b]		0.01286
	Interaction P-value [c]		0.14830

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Pyrexia	No. of Events (%)	55 (23.5)	38 (17.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (29.73, NC)
	Hazard Ratio (95% CI) [a]		1.337 (0.884, 2.022)
	Treatment P-value [b]		0.16564
	Interaction P-value [c]		0.30918
Infections and infestations	No. of Events (%)	126 (53.8)	86 (39.3)
	Median Survival Est. (95% CI)	4.76 (3.02, 11.33)	NC (10.41, NC)
	Hazard Ratio (95% CI) [a]		1.450 (1.102, 1.908)
	Treatment P-value [b]		0.00766
	Interaction P-value [c]		0.77404

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
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]		6.298 (1.430, 27.729)
	Treatment P-value [b]		0.00427
	Interaction P-value [c]		0.99837
Alanine aminotransferase increased	No. of Events (%)	23 (9.8)	6 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.540 (1.440, 8.703)
	Treatment P-value [b]		0.00336
	Interaction P-value [c]		0.76785

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Aspartate aminotransferase increased	No. of Events (%)	30 (12.8)	4 (1.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.176 (2.528, 20.375)
	Treatment P-value [b]		0.00002
	Interaction P-value [c]		0.49773
Blood creatinine increased	No. of Events (%)	19 (8.1)	6 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	30.62 (NC , NC)
	Hazard Ratio (95% CI) [a]		2.759 (1.098, 6.932)
	Treatment P-value [b]		0.02647
	Interaction P-value [c]		0.37380

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Neutrophil count decreased	No. of Events (%)	22 (9.4)	38 (17.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.478 (0.283, 0.809)
	Treatment P-value [b]		0.00566
	Interaction P-value [c]		0.40561
Weight decreased	No. of Events (%)	38 (16.2)	17 (7.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.130 (1.202, 3.775)
	Treatment P-value [b]		0.00785
	Interaction P-value [c]		0.57195

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
White blood cell count decreased	No. of Events (%)	12 (5.1)	19 (8.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.547 (0.266, 1.128)
	Treatment P-value [b]		0.10357
	Interaction P-value [c]		0.30744
Metabolism and nutrition disorders	No. of Events (%)	142 (60.7)	99 (45.2)
	Median Survival Est. (95% CI)	1.91 (1.35, 3.98)	25.33 (4.11, NC)
	Hazard Ratio (95% CI) [a]		1.393 (1.077, 1.801)
	Treatment P-value [b]		0.01023
	Interaction P-value [c]		0.94033

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Decreased appetite	No. of Events (%)	100 (42.7)	63 (28.8)
	Median Survival Est. (95% CI)	NC (6.37, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.497 (1.092, 2.052)
	Treatment P-value [b]		0.01139
	Interaction P-value [c]		0.96538
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

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Musculoskeletal and connective tissue disorders	No. of Events (%)	84 (35.9)	88 (40.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	28.32 (28.32, NC)
	Hazard Ratio (95% CI) [a]		0.782 (0.580, 1.055)
	Treatment P-value [b]		0.11214
	Interaction P-value [c]		0.31307
Arthralgia	No. of Events (%)	21 (9.0)	30 (13.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.585 (0.335, 1.022)
	Treatment P-value [b]		0.05563
	Interaction P-value [c]		0.54938

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Myalgia	No. of Events (%)	15 (6.4)	27 (12.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.476 (0.253, 0.896)
	Treatment P-value [b]		0.01915
	Interaction P-value [c]		0.98581
Nervous system disorders	No. of Events (%)	152 (65.0)	99 (45.2)
	Median Survival Est. (95% CI)	2.96 (2.27, 3.71)	8.61 (3.98, NC)
	Hazard Ratio (95% CI) [a]		1.594 (1.238, 2.054)
	Treatment P-value [b]		0.00023
	Interaction P-value [c]		0.18676

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Dysgeusia	No. of Events (%)	61 (26.1)	19 (8.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.212 (1.919, 5.375)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.83825
Peripheral motor neuropathy	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]		0.00202
	Interaction P-value [c]		0.99976

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Peripheral sensory neuropathy	No. of Events (%)	83 (35.5)	50 (22.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.481 (1.043, 2.104)
	Treatment P-value [b]		0.02740
	Interaction P-value [c]		0.87534
Depression	No. of Events (%)	11 (4.7)	1 (0.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.804 (1.265, 76.001)
	Treatment P-value [b]		0.00729
	Interaction P-value [c]		0.99279

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Renal and urinary disorders	No. of Events (%)	69 (29.5)	46 (21.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.371 (0.943, 1.991)
	Treatment P-value [b]		0.09587
	Interaction P-value [c]		0.56718
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	81 (34.6)	56 (25.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.342 (0.954, 1.887)
	Treatment P-value [b]		0.08520
	Interaction P-value [c]		0.69974

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Skin and subcutaneous tissue disorders	No. of Events (%)	191 (81.6)	110 (50.2)
	Median Survival Est. (95% CI)	0.62 (0.46, 0.82)	3.42 (1.61, NC)
	Hazard Ratio (95% CI) [a]		2.350 (1.856, 2.977)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.04483
Drug eruption	No. of Events (%)	19 (8.1)	5 (2.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.554 (1.326, 9.523)
	Treatment P-value [b]		0.00737
	Interaction P-value [c]		0.46138

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Dry skin	No. of Events (%)	45 (19.2)	10 (4.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.339 (2.186, 8.614)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.72414
Pruritus	No. of Events (%)	81 (34.6)	13 (5.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.965 (3.877, 12.513)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.16340

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Rash	No. of Events (%)	46 (19.7)	14 (6.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.116 (1.712, 5.671)
	Treatment P-value [b]		0.00007
	Interaction P-value [c]		0.09670
Rash maculo-papular	No. of Events (%)	41 (17.5)	1 (0.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		40.030 (5.514, 290.592)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.00758

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Skin hyperpigmentation	No. of Events (%)	16 (6.8)	1 (0.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (26.87, NC)
	Hazard Ratio (95% CI) [a]		14.866 (1.971, 112.121)
	Treatment P-value [b]		0.00049
	Interaction P-value [c]		0.46741

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Any Event	No. of Events (%)	59 (95.2)	72 (100.0)
	Median Survival Est. (95% CI)	0.18 (0.13, 0.26)	0.13 (0.10, 0.20)
	Hazard Ratio (95% CI) [a]		0.742 (0.525, 1.049)
	Treatment P-value [b]		0.12250
	Interaction P-value [c]		0.16730
Blood and lymphatic system disorders	No. of Events (%)	25 (40.3)	28 (38.9)
	Median Survival Est. (95% CI)	NC (4.86, NC)	NC (5.68, NC)
	Hazard Ratio (95% CI) [a]		1.007 (0.587, 1.727)
	Treatment P-value [b]		0.97057
	Interaction P-value [c]		0.01534

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		0.852 (0.475, 1.526)
	Treatment P-value [b]		0.58320
	Interaction P-value [c]		0.19653
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.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Eye disorders	No. of Events (%)	12 (19.4)	8 (11.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.869 (0.764, 4.573)
	Treatment P-value [b]		0.16435
	Interaction P-value [c]		0.12062
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]		4.841 (0.541, 43.309)
	Treatment P-value [b]		0.11810
	Interaction P-value [c]		0.75482

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Lacrimation increased	No. of Events (%)	3 (4.8)	3 (4.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.191 (0.240, 5.899)
	Treatment P-value [b]		0.82439
	Interaction P-value [c]		0.27881
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]		2.418 (0.219, 26.663)
	Treatment P-value [b]		0.46448
	Interaction P-value [c]		0.80602

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Diarrhoea	No. of Events (%)	21 (33.9)	22 (30.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (14.98, NC)
	Hazard Ratio (95% CI) [a]		1.143 (0.628, 2.078)
	Treatment P-value [b]		0.70329
	Interaction P-value [c]		0.27151
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, 23.270)
	Treatment P-value [b]		0.02367
	Interaction P-value [c]		0.60117

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		4.746 (0.530, 42.460)
	Treatment P-value [b]		0.11619
	Interaction P-value [c]		0.69649
Fatigue	No. of Events (%)	20 (32.3)	25 (34.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (18.07, NC)
	Hazard Ratio (95% CI) [a]		0.920 (0.511, 1.656)
	Treatment P-value [b]		0.81087
	Interaction P-value [c]		0.14830

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Pyrexia	No. of Events (%)	13 (21.0)	7 (9.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.256 (0.899, 5.657)
	Treatment P-value [b]		0.07984
	Interaction P-value [c]		0.30918
Infections and infestations	No. of Events (%)	31 (50.0)	25 (34.7)
	Median Survival Est. (95% CI)	8.64 (3.06, NC)	NC (17.68, NC)
	Hazard Ratio (95% CI) [a]		1.582 (0.934, 2.680)
	Treatment P-value [b]		0.07803
	Interaction P-value [c]		0.77404

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Conjunctivitis	No. of Events (%)	5 (8.1)	1 (1.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.280 (0.733, 53.776)
	Treatment P-value [b]		0.04590
	Interaction P-value [c]		0.99837
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]		5.059 (0.565, 45.292)
	Treatment P-value [b]		0.12075
	Interaction P-value [c]		0.76785

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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]		3.705 (0.748, 18.361)
	Treatment P-value [b]		0.08996
	Interaction P-value [c]		0.49773
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]		6.239 (1.340, 29.051)
	Treatment P-value [b]		0.01169
	Interaction P-value [c]		0.37380

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Neutrophil count decreased	No. of Events (%)	12 (19.4)	18 (25.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.700 (0.337, 1.454)
	Treatment P-value [b]		0.35089
	Interaction P-value [c]		0.40561
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]		3.093 (0.970, 9.865)
	Treatment P-value [b]		0.04736
	Interaction P-value [c]		0.57195

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
White blood cell count decreased	No. of Events (%)	4 (6.5)	15 (20.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.276 (0.091, 0.830)
	Treatment P-value [b]		0.01496
	Interaction P-value [c]		0.30744
Metabolism and nutrition disorders	No. of Events (%)	34 (54.8)	32 (44.4)
	Median Survival Est. (95% CI)	5.06 (1.25, NC)	16.59 (3.61, NC)
	Hazard Ratio (95% CI) [a]		1.364 (0.842, 2.211)
	Treatment P-value [b]		0.22989
	Interaction P-value [c]		0.94033

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Decreased appetite	No. of Events (%)	23 (37.1)	19 (26.4)
	Median Survival Est. (95% CI)	NC (7.52, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.474 (0.803, 2.706)
	Treatment P-value [b]		0.21278
	Interaction P-value [c]		0.96538
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

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Musculoskeletal and connective tissue disorders	No. of Events (%)	22 (35.5)	35 (48.6)
	Median Survival Est. (95% CI)	NC (6.60, NC)	14.85 (1.58, NC)
	Hazard Ratio (95% CI) [a]		0.571 (0.335, 0.973)
	Treatment P-value [b]		0.04674
	Interaction P-value [c]		0.31307
Arthralgia	No. of Events (%)	8 (12.9)	11 (15.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.810 (0.326, 2.015)
	Treatment P-value [b]		0.64999
	Interaction P-value [c]		0.54938

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Myalgia	No. of Events (%)	0	8 (11.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00804
	Interaction P-value [c]		0.98581
Nervous system disorders	No. of Events (%)	40 (64.5)	40 (55.6)
	Median Survival Est. (95% CI)	2.73 (1.45, 4.14)	2.40 (0.85, NC)
	Hazard Ratio (95% CI) [a]		1.134 (0.731, 1.758)
	Treatment P-value [b]		0.63299
	Interaction P-value [c]		0.18676

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		3.618 (1.303, 10.046)
	Treatment P-value [b]		0.00950
	Interaction P-value [c]		0.83825
Peripheral motor neuropathy	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]		0.21000
	Interaction P-value [c]		0.99976

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Peripheral sensory neuropathy	No. of Events (%)	22 (35.5)	18 (25.0)
	Median Survival Est. (95% CI)	NC (5.59, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.399 (0.750, 2.609)
	Treatment P-value [b]		0.26742
	Interaction P-value [c]		0.87534
Depression	No. of Events (%)	0	1 (1.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.35343
	Interaction P-value [c]		0.99279

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Renal and urinary disorders	No. of Events (%)	15 (24.2)	11 (15.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.764 (0.810, 3.840)
	Treatment P-value [b]		0.15749
	Interaction P-value [c]		0.56718
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	21 (33.9)	18 (25.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.545 (0.823, 2.900)
	Treatment P-value [b]		0.14618
	Interaction P-value [c]		0.69974

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Skin and subcutaneous tissue disorders	No. of Events (%)	47 (75.8)	45 (62.5)
	Median Survival Est. (95% CI)	0.66 (0.39, 0.99)	0.69 (0.66, 7.62)
	Hazard Ratio (95% CI) [a]		1.450 (0.963, 2.184)
	Treatment P-value [b]		0.07639
	Interaction P-value [c]		0.04483
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]		8.486 (1.044, 68.983)
	Treatment P-value [b]		0.01752
	Interaction P-value [c]		0.46138

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Dry skin	No. of Events (%)	8 (12.9)	3 (4.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.316 (0.879, 12.499)
	Treatment P-value [b]		0.06833
	Interaction P-value [c]		0.72414
Pruritus	No. of Events (%)	22 (35.5)	9 (12.5)
	Median Survival Est. (95% CI)	NC (7.92, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.490 (1.606, 7.581)
	Treatment P-value [b]		0.00085
	Interaction P-value [c]		0.16340

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Rash	No. of Events (%)	6 (9.7)	7 (9.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.085 (0.365, 3.230)
	Treatment P-value [b]		0.78675
	Interaction P-value [c]		0.09670
Rash maculo-papular	No. of Events (%)	11 (17.7)	7 (9.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.005 (0.777, 5.175)
	Treatment P-value [b]		0.13159
	Interaction P-value [c]		0.00758

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Skin hyperpigmentation	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]		4.921 (0.550, 44.051)
	Treatment P-value [b]		0.12191
	Interaction P-value [c]		0.46741

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)	0.21 (0.16, 0.26)	0.10 (0.07, 0.16)
	Hazard Ratio (95% CI) [a]		0.858 (0.666, 1.107)
	Treatment P-value [b]		0.35247
	Interaction P-value [c]		0.68988
Blood and lymphatic system disorders	No. of Events (%)	33 (27.0)	55 (44.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	16.59 (2.33, NC)
	Hazard Ratio (95% CI) [a]		0.474 (0.308, 0.731)
	Treatment P-value [b]		0.00047
	Interaction P-value [c]		0.06756

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Anaemia	No. of Events (%)	23 (18.9)	40 (32.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (22.97, NC)
	Hazard Ratio (95% CI) [a]		0.497 (0.297, 0.830)
	Treatment P-value [b]		0.00500
	Interaction P-value [c]		0.00777
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.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Eye disorders	No. of Events (%)	45 (36.9)	7 (5.7)
	Median Survival Est. (95% CI)	NC (6.90, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.626 (3.438, 16.915)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.04025
Lacrimation increased	No. of Events (%)	21 (17.2)	3 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.218 (2.153, 24.200)
	Treatment P-value [b]		0.00019
	Interaction P-value [c]		0.07698

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		8.701 (1.102, 68.680)
	Treatment P-value [b]		0.01333
	Interaction P-value [c]		0.42084
Diarrhoea	No. of Events (%)	52 (42.6)	26 (21.1)
	Median Survival Est. (95% CI)	NC (5.68, NC)	NC (25.56, NC)
	Hazard Ratio (95% CI) [a]		2.205 (1.377, 3.532)
	Treatment P-value [b]		0.00071
	Interaction P-value [c]		0.04330

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		2.005 (0.685, 5.867)
	Treatment P-value [b]		0.19556
	Interaction P-value [c]		0.85536
Chills	No. of Events (%)	8 (6.6)	1 (0.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.870 (0.984, 62.928)
	Treatment P-value [b]		0.02446
	Interaction P-value [c]		0.22538

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Fatigue	No. of Events (%)	44 (36.1)	34 (27.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.297 (0.829, 2.029)
	Treatment P-value [b]		0.24592
	Interaction P-value [c]		0.38466
Pyrexia	No. of Events (%)	27 (22.1)	12 (9.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	29.73 (29.73, NC)
	Hazard Ratio (95% CI) [a]		2.313 (1.172, 4.566)
	Treatment P-value [b]		0.01271
	Interaction P-value [c]		0.19557

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Infections and infestations	No. of Events (%)	67 (54.9)	57 (46.3)
	Median Survival Est. (95% CI)	3.94 (2.79, 11.33)	10.41 (3.78, NC)
	Hazard Ratio (95% CI) [a]		1.210 (0.850, 1.723)
	Treatment P-value [b]		0.29080
	Interaction P-value [c]		0.15673
Conjunctivitis	No. of Events (%)	13 (10.7)	2 (1.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.425 (1.450, 28.477)
	Treatment P-value [b]		0.00490
	Interaction P-value [c]		0.48694

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Alanine aminotransferase increased	No. of Events (%)	10 (8.2)	3 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.312 (0.911, 12.035)
	Treatment P-value [b]		0.05461
	Interaction P-value [c]		0.69278
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]		13.988 (1.840, 106.363)
	Treatment P-value [b]		0.00077
	Interaction P-value [c]		0.61280

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Blood creatinine increased	No. of Events (%)	8 (6.6)	4 (3.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	30.62 (30.62, NC)
	Hazard Ratio (95% CI) [a]		1.983 (0.597, 6.588)
	Treatment P-value [b]		0.21139
	Interaction P-value [c]		0.55917
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]		0.311 (0.100, 0.963)
	Treatment P-value [b]		0.02405
	Interaction P-value [c]		0.62194

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Weight decreased	No. of Events (%)	15 (12.3)	10 (8.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.476 (0.663, 3.285)
	Treatment P-value [b]		0.34883
	Interaction P-value [c]		0.38718
White blood cell 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]		0.135 (0.017, 1.101)
	Treatment P-value [b]		0.02147
	Interaction P-value [c]		0.21921

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Metabolism and nutrition disorders	No. of Events (%)	64 (52.5)	55 (44.7)
	Median Survival Est. (95% CI)	4.07 (2.10, NC)	25.33 (2.79, NC)
	Hazard Ratio (95% CI) [a]		1.101 (0.768, 1.579)
	Treatment P-value [b]		0.58139
	Interaction P-value [c]		0.16084
Decreased appetite	No. of Events (%)	42 (34.4)	37 (30.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (20.04, NC)
	Hazard Ratio (95% CI) [a]		1.069 (0.687, 1.663)
	Treatment P-value [b]		0.77206
	Interaction P-value [c]		0.10142

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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
Musculoskeletal and connective tissue disorders	No. of Events (%)	52 (42.6)	55 (44.7)
	Median Survival Est. (95% CI)	13.93 (4.86, NC)	28.32 (2.83, NC)
	Hazard Ratio (95% CI) [a]		0.840 (0.575, 1.227)
	Treatment P-value [b]		0.35574
	Interaction P-value [c]		0.42447

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Arthralgia	No. of Events (%)	18 (14.8)	18 (14.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.922 (0.480, 1.773)
	Treatment P-value [b]		0.77780
	Interaction P-value [c]		0.26718
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]		0.788 (0.353, 1.760)
	Treatment P-value [b]		0.57696
	Interaction P-value [c]		0.06638

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Nervous system disorders	No. of Events (%)	76 (62.3)	48 (39.0)
	Median Survival Est. (95% CI)	2.79 (2.00, 3.81)	NC (6.97, NC)
	Hazard Ratio (95% CI) [a]		1.837 (1.279, 2.639)
	Treatment P-value [b]		0.00086
	Interaction P-value [c]		0.24021
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]		4.268 (1.745, 10.438)
	Treatment P-value [b]		0.00052
	Interaction P-value [c]		0.25000

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Peripheral sensory neuropathy	No. of Events (%)	38 (31.1)	13 (10.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.061 (1.630, 5.746)
	Treatment P-value [b]		0.00027
	Interaction P-value [c]		0.01008
Renal and urinary disorders	No. of Events (%)	38 (31.1)	22 (17.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (25.26, NC)
	Hazard Ratio (95% CI) [a]		1.755 (1.038, 2.967)
	Treatment P-value [b]		0.03460
	Interaction P-value [c]		0.60684

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	37 (30.3)	30 (24.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.224 (0.756, 1.981)
	Treatment P-value [b]		0.40678
	Interaction P-value [c]		0.16558
Skin and subcutaneous tissue disorders	No. of Events (%)	89 (73.0)	51 (41.5)
	Median Survival Est. (95% CI)	1.02 (0.79, 1.18)	NC (3.12, NC)
	Hazard Ratio (95% CI) [a]		2.268 (1.606, 3.202)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.39897

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		3.916 (0.438, 35.038)
	Treatment P-value [b]		0.18411
	Interaction P-value [c]		0.99815
Dry skin	No. of Events (%)	22 (18.0)	3 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (26.94, NC)
	Hazard Ratio (95% CI) [a]		7.581 (2.269, 25.330)
	Treatment P-value [b]		0.00010
	Interaction P-value [c]		0.30600

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Pruritus	No. of Events (%)	29 (23.8)	3 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		10.675 (3.253, 35.031)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.29974
Rash	No. of Events (%)	30 (24.6)	6 (4.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.350 (2.226, 12.854)
	Treatment P-value [b]		0.00003
	Interaction P-value [c]		0.03556

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Rash maculo-papular	No. of Events (%)	11 (9.0)	1 (0.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		10.888 (1.406, 84.337)
	Treatment P-value [b]		0.00509
	Interaction P-value [c]		0.80074
Skin hyperpigmentation	No. of Events (%)	2 (1.6)	1 (0.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (26.87, NC)
	Hazard Ratio (95% CI) [a]		1.948 (0.177, 21.486)
	Treatment P-value [b]		0.60480
	Interaction P-value [c]		0.81028

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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 (0.563, 1.355)
	Treatment P-value [b]		0.39603
	Interaction P-value [c]		0.68988
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]		0.313 (0.148, 0.661)
	Treatment P-value [b]		0.00178
	Interaction P-value [c]		0.06756

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		0.195 (0.072, 0.525)
	Treatment P-value [b]		0.00061
	Interaction P-value [c]		0.00777
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.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Eye disorders	No. of Events (%)	17 (40.5)	9 (23.1)
	Median Survival Est. (95% CI)	NC (3.94, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.999 (0.891, 4.485)
	Treatment P-value [b]		0.07931
	Interaction P-value [c]		0.04025
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]		0.07698

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		2.793 (0.290, 26.850)
	Treatment P-value [b]		0.36367
	Interaction P-value [c]		0.42084
Diarrhoea	No. of Events (%)	14 (33.3)	16 (41.0)
	Median Survival Est. (95% CI)	NC (15.97, NC)	NC (2.69, NC)
	Hazard Ratio (95% CI) [a]		0.749 (0.366, 1.536)
	Treatment P-value [b]		0.44917
	Interaction P-value [c]		0.04330

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		0.85536
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]		0.934 (0.270, 3.225)
	Treatment P-value [b]		0.91152
	Interaction P-value [c]		0.22538

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		0.931 (0.489, 1.774)
	Treatment P-value [b]		0.83217
	Interaction P-value [c]		0.38466
Pyrexia	No. of Events (%)	7 (16.7)	8 (20.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.798 (0.289, 2.201)
	Treatment P-value [b]		0.66346
	Interaction P-value [c]		0.19557

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		2.486 (1.277, 4.839)
	Treatment P-value [b]		0.00790
	Interaction P-value [c]		0.15673
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]		0.936 (0.059, 14.972)
	Treatment P-value [b]		0.95956
	Interaction P-value [c]		0.48694

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		2.358 (0.457, 12.159)
	Treatment P-value [b]		0.27678
	Interaction P-value [c]		0.69278
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]		4.523 (0.977, 20.934)
	Treatment P-value [b]		0.03132
	Interaction P-value [c]		0.61280

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		4.018 (0.860, 18.775)
	Treatment P-value [b]		0.03441
	Interaction P-value [c]		0.55917
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]		0.619 (0.215, 1.784)
	Treatment P-value [b]		0.38516
	Interaction P-value [c]		0.62194

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		3.035 (0.979, 9.412)
	Treatment P-value [b]		0.04841
	Interaction P-value [c]		0.38718
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]		1.201 (0.269, 5.366)
	Treatment P-value [b]		0.80009
	Interaction P-value [c]		0.21921

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Metabolism and nutrition disorders	No. of Events (%)	30 (71.4)	24 (61.5)
	Median Survival Est. (95% CI)	0.90 (0.46, 2.17)	1.74 (0.69, NC)
	Hazard Ratio (95% CI) [a]		1.303 (0.762, 2.230)
	Treatment P-value [b]		0.37130
	Interaction P-value [c]		0.16084
Decreased appetite	No. of Events (%)	19 (45.2)	13 (33.3)
	Median Survival Est. (95% CI)	NC (2.10, NC)	NC (7.23, NC)
	Hazard Ratio (95% CI) [a]		1.409 (0.696, 2.853)
	Treatment P-value [b]		0.37843
	Interaction P-value [c]		0.10142

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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
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]		0.504 (0.256, 0.992)
	Treatment P-value [b]		0.05629
	Interaction P-value [c]		0.42447

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Arthralgia	No. of Events (%)	4 (9.5)	9 (23.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.377 (0.116, 1.225)
	Treatment P-value [b]		0.10090
	Interaction P-value [c]		0.26718
Myalgia	No. of Events (%)	1 (2.4)	4 (10.3)
	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]		0.15833
	Interaction P-value [c]		0.06638

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		1.149 (0.672, 1.966)
	Treatment P-value [b]		0.65160
	Interaction P-value [c]		0.24021
Dysgeusia	No. of Events (%)	14 (33.3)	8 (20.5)
	Median Survival Est. (95% CI)	NC (5.55, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.714 (0.719, 4.086)
	Treatment P-value [b]		0.22232
	Interaction P-value [c]		0.25000

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		1.505 (0.683, 3.316)
	Treatment P-value [b]		0.30103
	Interaction P-value [c]		0.01008
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]		0.60684

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	21 (50.0)	21 (53.8)
	Median Survival Est. (95% CI)	5.82 (1.87, NC)	5.52 (2.56, NC)
	Hazard Ratio (95% CI) [a]		0.962 (0.525, 1.763)
	Treatment P-value [b]		0.93191
	Interaction P-value [c]		0.16558
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]		1.543 (0.929, 2.565)
	Treatment P-value [b]		0.07453
	Interaction P-value [c]		0.39897

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		0.99815
Dry skin	No. of Events (%)	14 (33.3)	3 (7.7)
	Median Survival Est. (95% CI)	NC (5.55, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.876 (1.400, 16.984)
	Treatment P-value [b]		0.00471
	Interaction P-value [c]		0.30600

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		8.101 (2.406, 27.274)
	Treatment P-value [b]		0.00005
	Interaction P-value [c]		0.29974
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]		0.679 (0.152, 3.034)
	Treatment P-value [b]		0.58534
	Interaction P-value [c]		0.03556

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		8.128 (2.413, 27.376)
	Treatment P-value [b]		0.00005
	Interaction P-value [c]		0.80074
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]		5.622 (0.675, 46.852)
	Treatment P-value [b]		0.05908
	Interaction P-value [c]		0.81028

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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]		0.68988
Blood and lymphatic system disorders	No. of Events (%)	44 (33.3)	51 (39.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (7.85, NC)
	Hazard Ratio (95% CI) [a]		0.776 (0.518, 1.161)
	Treatment P-value [b]		0.22080
	Interaction P-value [c]		0.06756

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Anaemia	No. of Events (%)	34 (25.8)	33 (25.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.996 (0.617, 1.608)
	Treatment P-value [b]		0.99690
	Interaction P-value [c]		0.00777
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.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Eye disorders	No. of Events (%)	24 (18.2)	10 (7.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.407 (1.151, 5.033)
	Treatment P-value [b]		0.01642
	Interaction P-value [c]		0.04025
Lacrimation increased	No. of Events (%)	7 (5.3)	4 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.644 (0.481, 5.619)
	Treatment P-value [b]		0.42725
	Interaction P-value [c]		0.07698

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	5 (3.8)	3 (2.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.610 (0.385, 6.740)
	Treatment P-value [b]		0.52649
	Interaction P-value [c]		0.42084
Diarrhoea	No. of Events (%)	40 (30.3)	28 (21.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.380 (0.851, 2.237)
	Treatment P-value [b]		0.18874
	Interaction P-value [c]		0.04330

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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]		0.85536
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]		0.22538

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	47 (35.6)	29 (22.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.626 (1.024, 2.584)
	Treatment P-value [b]		0.04234
	Interaction P-value [c]		0.38466
Pyrexia	No. of Events (%)	34 (25.8)	25 (19.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.321 (0.788, 2.215)
	Treatment P-value [b]		0.29629
	Interaction P-value [c]		0.19557

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Infections and infestations	No. of Events (%)	64 (48.5)	41 (31.8)
	Median Survival Est. (95% CI)	10.87 (3.55, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.592 (1.076, 2.357)
	Treatment P-value [b]		0.02163
	Interaction P-value [c]		0.15673
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]		0.02989
	Interaction P-value [c]		0.48694

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Alanine aminotransferase increased	No. of Events (%)	12 (9.1)	2 (1.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.056 (1.355, 27.065)
	Treatment P-value [b]		0.00753
	Interaction P-value [c]		0.69278
Aspartate aminotransferase increased	No. of Events (%)	13 (9.8)	3 (2.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.474 (1.275, 15.704)
	Treatment P-value [b]		0.01181
	Interaction P-value [c]		0.61280

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Blood creatinine increased	No. of Events (%)	11 (8.3)	2 (1.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.420 (1.201, 24.460)
	Treatment P-value [b]		0.01611
	Interaction P-value [c]		0.55917
Neutrophil count decreased	No. of Events (%)	24 (18.2)	36 (27.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.552 (0.329, 0.925)
	Treatment P-value [b]		0.02635
	Interaction P-value [c]		0.62194

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
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]		3.122 (1.327, 7.346)
	Treatment P-value [b]		0.00603
	Interaction P-value [c]		0.38718
White blood cell count decreased	No. of Events (%)	11 (8.3)	24 (18.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.393 (0.192, 0.803)
	Treatment P-value [b]		0.00958
	Interaction P-value [c]		0.21921

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Metabolism and nutrition disorders	No. of Events (%)	82 (62.1)	52 (40.3)
	Median Survival Est. (95% CI)	1.87 (1.05, 5.06)	NC (14.92, NC)
	Hazard Ratio (95% CI) [a]		1.786 (1.261, 2.530)
	Treatment P-value [b]		0.00102
	Interaction P-value [c]		0.16084
Decreased appetite	No. of Events (%)	62 (47.0)	32 (24.8)
	Median Survival Est. (95% CI)	NC (4.11, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.086 (1.361, 3.197)
	Treatment P-value [b]		0.00057
	Interaction P-value [c]		0.10142

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
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
Musculoskeletal and connective tissue disorders	No. of Events (%)	40 (30.3)	47 (36.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (16.30, NC)
	Hazard Ratio (95% CI) [a]		0.698 (0.458, 1.065)
	Treatment P-value [b]		0.09381
	Interaction P-value [c]		0.42447

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Arthralgia	No. of Events (%)	7 (5.3)	14 (10.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.439 (0.177, 1.087)
	Treatment P-value [b]		0.07048
	Interaction P-value [c]		0.26718
Myalgia	No. of Events (%)	3 (2.3)	18 (14.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.148 (0.044, 0.502)
	Treatment P-value [b]		0.00039
	Interaction P-value [c]		0.06638

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Nervous system disorders	No. of Events (%)	86 (65.2)	67 (51.9)
	Median Survival Est. (95% CI)	3.09 (2.00, 4.07)	4.53 (2.40, NC)
	Hazard Ratio (95% CI) [a]		1.293 (0.940, 1.780)
	Treatment P-value [b]		0.10479
	Interaction P-value [c]		0.24021
Dysgeusia	No. of Events (%)	37 (28.0)	10 (7.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.998 (1.988, 8.041)
	Treatment P-value [b]		0.00003
	Interaction P-value [c]		0.25000

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Peripheral sensory neuropathy	No. of Events (%)	51 (38.6)	45 (34.9)
	Median Survival Est. (95% CI)	NC (6.60, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.968 (0.648, 1.445)
	Treatment P-value [b]		0.87593
	Interaction P-value [c]		0.01008
Renal and urinary disorders	No. of Events (%)	32 (24.2)	26 (20.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.205 (0.718, 2.023)
	Treatment P-value [b]		0.49826
	Interaction P-value [c]		0.60684

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	44 (33.3)	23 (17.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.985 (1.199, 3.288)
	Treatment P-value [b]		0.00615
	Interaction P-value [c]		0.16558
Skin and subcutaneous tissue disorders	No. of Events (%)	114 (86.4)	78 (60.5)
	Median Survival Est. (95% CI)	0.39 (0.33, 0.49)	0.72 (0.69, 2.37)
	Hazard Ratio (95% CI) [a]		2.260 (1.692, 3.019)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.39897

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)	5 (3.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.642 (1.352, 9.813)
	Treatment P-value [b]		0.00679
	Interaction P-value [c]		0.99815
Dry skin	No. of Events (%)	17 (12.9)	7 (5.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.446 (1.014, 5.900)
	Treatment P-value [b]		0.04040
	Interaction P-value [c]		0.30600

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)	16 (12.4)
	Median Survival Est. (95% CI)	NC (7.92, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.243 (2.428, 7.416)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.29974
Rash	No. of Events (%)	19 (14.4)	11 (8.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.731 (0.823, 3.639)
	Treatment P-value [b]		0.14427
	Interaction P-value [c]		0.03556

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	21 (15.9)	4 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.459 (1.874, 15.907)
	Treatment P-value [b]		0.00057
	Interaction P-value [c]		0.80074
Skin hyperpigmentation	No. of Events (%)	12 (9.1)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00047
	Interaction P-value [c]		0.81028

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		1.040 (0.804, 1.345)
	Treatment P-value [b]		0.73465
	Interaction P-value [c]		0.20546
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]		0.548 (0.339, 0.887)
	Treatment P-value [b]		0.01444
	Interaction P-value [c]		0.98109

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Anaemia	No. of Events (%)	17 (14.2)	34 (28.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.442 (0.247, 0.791)
	Treatment P-value [b]		0.00556
	Interaction P-value [c]		0.20245
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.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Eye disorders	No. of Events (%)	33 (27.5)	10 (8.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.700 (1.824, 7.508)
	Treatment P-value [b]		0.00009
	Interaction P-value [c]		0.88076
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]		1.511 (0.252, 9.041)
	Treatment P-value [b]		0.64252
	Interaction P-value [c]		0.08366

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Lacrimation increased	No. of Events (%)	13 (10.8)	4 (3.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.388 (1.105, 10.391)
	Treatment P-value [b]		0.02423
	Interaction P-value [c]		0.63182
Vision blurred	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]		7.120 (0.876, 57.875)
	Treatment P-value [b]		0.03294
	Interaction P-value [c]		0.35437

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Diarrhoea	No. of Events (%)	43 (35.8)	32 (26.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.340 (0.848, 2.118)
	Treatment P-value [b]		0.22288
	Interaction P-value [c]		0.48097
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]		3.781 (1.055, 13.552)
	Treatment P-value [b]		0.02921
	Interaction P-value [c]		0.84719

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Chills	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]		9.119 (1.155, 71.968)
	Treatment P-value [b]		0.01065
	Interaction P-value [c]		0.21188
Fatigue	No. of Events (%)	39 (32.5)	39 (32.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.946 (0.607, 1.475)
	Treatment P-value [b]		0.78096
	Interaction P-value [c]		0.04577

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Pyrexia	No. of Events (%)	26 (21.7)	17 (14.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.570 (0.852, 2.894)
	Treatment P-value [b]		0.15070
	Interaction P-value [c]		0.81708
Infections and infestations	No. of Events (%)	63 (52.5)	38 (31.9)
	Median Survival Est. (95% CI)	7.82 (3.52, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.807 (1.208, 2.703)
	Treatment P-value [b]		0.00382
	Interaction P-value [c]		0.21969

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		0.00133
	Interaction P-value [c]		0.98755
Alanine aminotransferase increased	No. of Events (%)	15 (12.5)	2 (1.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		8.008 (1.832, 35.012)
	Treatment P-value [b]		0.00104
	Interaction P-value [c]		0.16940

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Aspartate aminotransferase increased	No. of Events (%)	19 (15.8)	1 (0.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		20.985 (2.813, 156.572)
	Treatment P-value [b]		0.00003
	Interaction P-value [c]		0.10267
Blood creatinine increased	No. of Events (%)	11 (9.2)	1 (0.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		11.431 (1.475, 88.583)
	Treatment P-value [b]		0.00417
	Interaction P-value [c]		0.15077

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Neutrophil count decreased	No. of Events (%)	17 (14.2)	32 (26.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.455 (0.253, 0.819)
	Treatment P-value [b]		0.00846
	Interaction P-value [c]		0.46479
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]		2.171 (0.937, 5.032)
	Treatment P-value [b]		0.06266
	Interaction P-value [c]		0.85368

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
White blood cell count decreased	No. of Events (%)	10 (8.3)	18 (15.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.505 (0.233, 1.093)
	Treatment P-value [b]		0.08277
	Interaction P-value [c]		0.51443
Metabolism and nutrition disorders	No. of Events (%)	59 (49.2)	46 (38.7)
	Median Survival Est. (95% CI)	9.56 (2.04, NC)	NC (18.63, NC)
	Hazard Ratio (95% CI) [a]		1.344 (0.914, 1.976)
	Treatment P-value [b]		0.14813
	Interaction P-value [c]		0.82065

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Decreased appetite	No. of Events (%)	41 (34.2)	30 (25.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.397 (0.872, 2.238)
	Treatment P-value [b]		0.17079
	Interaction P-value [c]		0.71707
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

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Musculoskeletal and connective tissue disorders	No. of Events (%)	43 (35.8)	51 (42.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (5.68, NC)
	Hazard Ratio (95% CI) [a]		0.731 (0.487, 1.098)
	Treatment P-value [b]		0.13378
	Interaction P-value [c]		0.92510
Arthralgia	No. of Events (%)	12 (10.0)	16 (13.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.705 (0.333, 1.490)
	Treatment P-value [b]		0.37481
	Interaction P-value [c]		0.69645

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Myalgia	No. of Events (%)	6 (5.0)	13 (10.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.435 (0.165, 1.144)
	Treatment P-value [b]		0.08109
	Interaction P-value [c]		0.76983
Nervous system disorders	No. of Events (%)	88 (73.3)	64 (53.8)
	Median Survival Est. (95% CI)	2.56 (1.51, 3.68)	4.86 (2.14, NC)
	Hazard Ratio (95% CI) [a]		1.538 (1.114, 2.124)
	Treatment P-value [b]		0.00871
	Interaction P-value [c]		0.69231

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		3.636 (1.904, 6.947)
	Treatment P-value [b]		0.00004
	Interaction P-value [c]		0.71650
Peripheral sensory neuropathy	No. of Events (%)	49 (40.8)	39 (32.8)
	Median Survival Est. (95% CI)	NC (8.34, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.189 (0.781, 1.812)
	Treatment P-value [b]		0.41588
	Interaction P-value [c]		0.17600

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Renal and urinary disorders	No. of Events (%)	30 (25.0)	18 (15.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.736 (0.968, 3.115)
	Treatment P-value [b]		0.06367
	Interaction P-value [c]		0.44578
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	35 (29.2)	25 (21.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.470 (0.880, 2.457)
	Treatment P-value [b]		0.13787
	Interaction P-value [c]		0.76660

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Skin and subcutaneous tissue disorders	No. of Events (%)	103 (85.8)	66 (55.5)
	Median Survival Est. (95% CI)	0.38 (0.33, 0.49)	2.86 (0.72, NC)
	Hazard Ratio (95% CI) [a]		2.547 (1.866, 3.477)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.12441
Drug eruption	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]		3.842 (1.426, 10.348)
	Treatment P-value [b]		0.00486
	Interaction P-value [c]		0.56311

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Dry skin	No. of Events (%)	20 (16.7)	5 (4.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.251 (1.596, 11.328)
	Treatment P-value [b]		0.00167
	Interaction P-value [c]		0.95181
Pruritus	No. of Events (%)	49 (40.8)	12 (10.1)
	Median Survival Est. (95% CI)	NC (5.55, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.097 (2.710, 9.587)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.69362

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Rash	No. of Events (%)	22 (18.3)	9 (7.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.586 (1.190, 5.615)
	Treatment P-value [b]		0.01353
	Interaction P-value [c]		0.92119
Rash maculo-papular	No. of Events (%)	26 (21.7)	3 (2.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.663 (2.924, 31.928)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.41712

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		0.98966

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		0.839 (0.679, 1.036)
	Treatment P-value [b]		0.10010
	Interaction P-value [c]		0.20546
Blood and lymphatic system disorders	No. of Events (%)	60 (34.1)	85 (49.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	7.26 (2.33, 22.97)
	Hazard Ratio (95% CI) [a]		0.552 (0.396, 0.768)
	Treatment P-value [b]		0.00031
	Interaction P-value [c]		0.98109

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Anaemia	No. of Events (%)	45 (25.6)	57 (33.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (22.97, NC)
	Hazard Ratio (95% CI) [a]		0.697 (0.471, 1.031)
	Treatment P-value [b]		0.06367
	Interaction P-value [c]		0.20245
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.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Eye disorders	No. of Events (%)	53 (30.1)	16 (9.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.453 (1.974, 6.041)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.88076
Dry eye	No. of Events (%)	17 (9.7)	1 (0.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		16.317 (2.171, 122.646)
	Treatment P-value [b]		0.00024
	Interaction P-value [c]		0.08366

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Lacrimation increased	No. of Events (%)	21 (11.9)	8 (4.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.415 (1.069, 5.454)
	Treatment P-value [b]		0.02594
	Interaction P-value [c]		0.63182
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]		2.296 (0.720, 7.325)
	Treatment P-value [b]		0.14770
	Interaction P-value [c]		0.35437

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Diarrhoea	No. of Events (%)	63 (35.8)	38 (22.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (25.56, NC)
	Hazard Ratio (95% CI) [a]		1.669 (1.115, 2.497)
	Treatment P-value [b]		0.01096
	Interaction P-value [c]		0.48097
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]		3.199 (1.043, 9.813)
	Treatment P-value [b]		0.03118
	Interaction P-value [c]		0.84719

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	11 (6.3)	5 (2.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.079 (0.722, 5.990)
	Treatment P-value [b]		0.17148
	Interaction P-value [c]		0.21188
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]		1.719 (1.173, 2.517)
	Treatment P-value [b]		0.00450
	Interaction P-value [c]		0.04577

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Pyrexia	No. of Events (%)	42 (23.9)	28 (16.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	29.73 (NC , NC)
	Hazard Ratio (95% CI) [a]		1.433 (0.888, 2.312)
	Treatment P-value [b]		0.14346
	Interaction P-value [c]		0.81708
Infections and infestations	No. of Events (%)	94 (53.4)	73 (42.4)
	Median Survival Est. (95% CI)	3.94 (2.73, 10.87)	14.88 (5.52, NC)
	Hazard Ratio (95% CI) [a]		1.316 (0.969, 1.787)
	Treatment P-value [b]		0.08572
	Interaction P-value [c]		0.21969

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Conjunctivitis	No. of Events (%)	9 (5.1)	3 (1.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.782 (0.752, 10.284)
	Treatment P-value [b]		0.11718
	Interaction P-value [c]		0.98755
Alanine aminotransferase increased	No. of Events (%)	12 (6.8)	5 (2.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.256 (0.794, 6.407)
	Treatment P-value [b]		0.11750
	Interaction P-value [c]		0.16940

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		3.240 (1.195, 8.784)
	Treatment P-value [b]		0.01415
	Interaction P-value [c]		0.10267
Blood creatinine increased	No. of Events (%)	17 (9.7)	7 (4.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	30.62 (NC , NC)
	Hazard Ratio (95% CI) [a]		2.229 (0.922, 5.387)
	Treatment P-value [b]		0.06155
	Interaction P-value [c]		0.15077

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Neutrophil count decreased	No. of Events (%)	17 (9.7)	24 (14.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.626 (0.336, 1.166)
	Treatment P-value [b]		0.11804
	Interaction P-value [c]		0.46479
Weight decreased	No. of Events (%)	31 (17.6)	13 (7.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.399 (1.255, 4.585)
	Treatment P-value [b]		0.00642
	Interaction P-value [c]		0.85368

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
White blood cell count decreased	No. of Events (%)	6 (3.4)	16 (9.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.337 (0.132, 0.861)
	Treatment P-value [b]		0.01591
	Interaction P-value [c]		0.51443
Metabolism and nutrition disorders	No. of Events (%)	117 (66.5)	85 (49.4)
	Median Survival Est. (95% CI)	1.71 (1.02, 2.89)	5.29 (2.60, NC)
	Hazard Ratio (95% CI) [a]		1.420 (1.074, 1.878)
	Treatment P-value [b]		0.01218
	Interaction P-value [c]		0.82065

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Decreased appetite	No. of Events (%)	82 (46.6)	52 (30.2)
	Median Survival Est. (95% CI)	NC (4.11, NC)	NC (20.04, NC)
	Hazard Ratio (95% CI) [a]		1.557 (1.100, 2.204)
	Treatment P-value [b]		0.01175
	Interaction P-value [c]		0.71707
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

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Musculoskeletal and connective tissue disorders	No. of Events (%)	63 (35.8)	72 (41.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	28.32 (4.27, NC)
	Hazard Ratio (95% CI) [a]		0.713 (0.508, 1.000)
	Treatment P-value [b]		0.05374
	Interaction P-value [c]		0.92510
Arthralgia	No. of Events (%)	17 (9.7)	25 (14.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.581 (0.314, 1.077)
	Treatment P-value [b]		0.06674
	Interaction P-value [c]		0.69645

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Myalgia	No. of Events (%)	9 (5.1)	22 (12.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.361 (0.166, 0.785)
	Treatment P-value [b]		0.00835
	Interaction P-value [c]		0.76983
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]		1.408 (1.046, 1.895)
	Treatment P-value [b]		0.02139
	Interaction P-value [c]		0.69231

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Dysgeusia	No. of Events (%)	36 (20.5)	12 (7.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.067 (1.595, 5.895)
	Treatment P-value [b]		0.00042
	Interaction P-value [c]		0.71650
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]		1.819 (1.161, 2.848)
	Treatment P-value [b]		0.00783
	Interaction P-value [c]		0.17600

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Renal and urinary disorders	No. of Events (%)	54 (30.7)	39 (22.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (25.26, NC)
	Hazard Ratio (95% CI) [a]		1.315 (0.870, 1.985)
	Treatment P-value [b]		0.19081
	Interaction P-value [c]		0.44578
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	67 (38.1)	49 (28.5)
	Median Survival Est. (95% CI)	NC (6.64, NC)	NC (21.29, NC)
	Hazard Ratio (95% CI) [a]		1.336 (0.924, 1.931)
	Treatment P-value [b]		0.12704
	Interaction P-value [c]		0.76660

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Skin and subcutaneous tissue disorders	No. of Events (%)	135 (76.7)	89 (51.7)
	Median Survival Est. (95% CI)	0.89 (0.66, 0.99)	3.02 (1.31, NC)
	Hazard Ratio (95% CI) [a]		1.848 (1.413, 2.416)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.12441
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]		7.579 (0.948, 60.607)
	Treatment P-value [b]		0.02459
	Interaction P-value [c]		0.56311

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Dry skin	No. of Events (%)	33 (18.8)	8 (4.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (26.94, NC)
	Hazard Ratio (95% CI) [a]		4.091 (1.889, 8.861)
	Treatment P-value [b]		0.00011
	Interaction P-value [c]		0.95181
Pruritus	No. of Events (%)	54 (30.7)	10 (5.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.137 (3.126, 12.051)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.69362

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)	12 (7.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.455 (1.256, 4.798)
	Treatment P-value [b]		0.00571
	Interaction P-value [c]		0.92119
Rash maculo-papular	No. of Events (%)	26 (14.8)	5 (2.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.126 (1.968, 13.353)
	Treatment P-value [b]		0.00016
	Interaction P-value [c]		0.41712

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Skin hyperpigmentation	No. of Events (%)	7 (4.0)	2 (1.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (26.87, NC)
	Hazard Ratio (95% CI) [a]		3.295 (0.683, 15.889)
	Treatment P-value [b]		0.14099
	Interaction P-value [c]		0.98966

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Any Event	No. of Events (%)	90 (97.8)	84 (96.6)
	Median Survival Est. (95% CI)	0.16 (0.10, 0.23)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		1.125 (0.834, 1.516)
	Treatment P-value [b]		0.61554
	Interaction P-value [c]		0.10953
Blood and lymphatic system disorders	No. of Events (%)	30 (32.6)	37 (42.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (2.14, NC)
	Hazard Ratio (95% CI) [a]		0.681 (0.420, 1.102)
	Treatment P-value [b]		0.12629
	Interaction P-value [c]		0.33993

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Anaemia	No. of Events (%)	20 (21.7)	24 (27.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.761 (0.420, 1.378)
	Treatment P-value [b]		0.40295
	Interaction P-value [c]		0.36310
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.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		2.893 (1.223, 6.844)
	Treatment P-value [b]		0.01007
	Interaction P-value [c]		0.58214
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]		0.99028

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		3.173 (0.659, 15.270)
	Treatment P-value [b]		0.11968
	Interaction P-value [c]		0.85675
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]		2.140 (0.553, 8.281)
	Treatment P-value [b]		0.24898
	Interaction P-value [c]		0.42650

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Diarrhoea	No. of Events (%)	28 (30.4)	18 (20.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.514 (0.837, 2.738)
	Treatment P-value [b]		0.16683
	Interaction P-value [c]		0.98670
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]		1.713 (0.501, 5.855)
	Treatment P-value [b]		0.39088
	Interaction P-value [c]		0.17214

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		1.547 (0.370, 6.479)
	Treatment P-value [b]		0.49822
	Interaction P-value [c]		0.22773
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]		1.256 (0.740, 2.133)
	Treatment P-value [b]		0.35598
	Interaction P-value [c]		0.77856

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Pyrexia	No. of Events (%)	19 (20.7)	17 (19.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.025 (0.533, 1.972)
	Treatment P-value [b]		0.90927
	Interaction P-value [c]		0.18028
Infections and infestations	No. of Events (%)	47 (51.1)	32 (36.8)
	Median Survival Est. (95% CI)	6.60 (2.17, NC)	17.97 (17.68, NC)
	Hazard Ratio (95% CI) [a]		1.464 (0.934, 2.294)
	Treatment P-value [b]		0.11124
	Interaction P-value [c]		0.93705

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Conjunctivitis	No. of Events (%)	10 (10.9)	2 (2.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.662 (1.021, 21.293)
	Treatment P-value [b]		0.03607
	Interaction P-value [c]		0.62334
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]		3.213 (0.667, 15.474)
	Treatment P-value [b]		0.11544
	Interaction P-value [c]		0.79639

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		4.220 (0.912, 19.538)
	Treatment P-value [b]		0.04628
	Interaction P-value [c]		0.58540
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]		3.169 (0.657, 15.276)
	Treatment P-value [b]		0.10743
	Interaction P-value [c]		0.91656

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Neutrophil count decreased	No. of Events (%)	13 (14.1)	13 (14.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.870 (0.403, 1.877)
	Treatment P-value [b]		0.70653
	Interaction P-value [c]		0.13208
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]		1.242 (0.523, 2.949)
	Treatment P-value [b]		0.60578
	Interaction P-value [c]		0.09334

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
White blood cell count decreased	No. of Events (%)	2 (2.2)	5 (5.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.360 (0.070, 1.856)
	Treatment P-value [b]		0.20043
	Interaction P-value [c]		0.83138
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]		1.579 (1.041, 2.396)
	Treatment P-value [b]		0.03144
	Interaction P-value [c]		0.48971

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		1.529 (0.925, 2.527)
	Treatment P-value [b]		0.09160
	Interaction P-value [c]		0.93498
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.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	27 (29.3)	37 (42.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	16.30 (2.30, NC)
	Hazard Ratio (95% CI) [a]		0.592 (0.361, 0.973)
	Treatment P-value [b]		0.03416
	Interaction P-value [c]		0.35310
Arthralgia	No. of Events (%)	8 (8.7)	9 (10.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.780 (0.301, 2.021)
	Treatment P-value [b]		0.60252
	Interaction P-value [c]		0.61829

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Myalgia	No. of Events (%)	2 (2.2)	11 (12.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.159 (0.035, 0.717)
	Treatment P-value [b]		0.00485
	Interaction P-value [c]		0.17271
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]		1.098 (0.724, 1.666)
	Treatment P-value [b]		0.64068
	Interaction P-value [c]		0.11038

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Dysgeusia	No. of Events (%)	16 (17.4)	8 (9.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.914 (0.819, 4.473)
	Treatment P-value [b]		0.13293
	Interaction P-value [c]		0.14228
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]		1.408 (0.739, 2.685)
	Treatment P-value [b]		0.30225
	Interaction P-value [c]		0.88792

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Depression	No. of Events (%)	1 (1.1)	1 (1.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.892 (0.056, 14.276)
	Treatment P-value [b]		0.96669
	Interaction P-value [c]		0.17361
Renal and urinary disorders	No. of Events (%)	20 (21.7)	15 (17.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.256 (0.643, 2.454)
	Treatment P-value [b]		0.48963
	Interaction P-value [c]		0.60470

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	32 (34.8)	21 (24.1)
	Median Survival Est. (95% CI)	NC (5.13, NC)	NC (21.29, NC)
	Hazard Ratio (95% CI) [a]		1.526 (0.880, 2.646)
	Treatment P-value [b]		0.13334
	Interaction P-value [c]		0.69514
Skin and subcutaneous tissue disorders	No. of Events (%)	66 (71.7)	46 (52.9)
	Median Survival Est. (95% CI)	0.62 (0.39, 0.95)	2.37 (1.12, NC)
	Hazard Ratio (95% CI) [a]		1.913 (1.312, 2.790)
	Treatment P-value [b]		0.00075
	Interaction P-value [c]		0.58547

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Drug eruption	No. of Events (%)	8 (8.7)	3 (3.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.522 (0.669, 9.509)
	Treatment P-value [b]		0.15433
	Interaction P-value [c]		0.33916
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]		2.886 (1.048, 7.945)
	Treatment P-value [b]		0.02555
	Interaction P-value [c]		0.40018

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Pruritus	No. of Events (%)	32 (34.8)	7 (8.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.323 (2.349, 12.063)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.91188
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]		1.822 (0.623, 5.333)
	Treatment P-value [b]		0.24602
	Interaction P-value [c]		0.49566

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		0.99460
Rash maculo-papular	No. of Events (%)	18 (19.6)	3 (3.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.184 (1.821, 21.008)
	Treatment P-value [b]		0.00083
	Interaction P-value [c]		0.86307

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		0.99187

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		0.840 (0.691, 1.022)
	Treatment P-value [b]		0.08397
	Interaction P-value [c]		0.10953
Blood and lymphatic system disorders	No. of Events (%)	57 (27.9)	91 (44.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	22.97 (5.55, NC)
	Hazard Ratio (95% CI) [a]		0.512 (0.368, 0.713)
	Treatment P-value [b]		0.00005
	Interaction P-value [c]		0.33993

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Anaemia	No. of Events (%)	42 (20.6)	67 (32.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.548 (0.372, 0.806)
	Treatment P-value [b]		0.00169
	Interaction P-value [c]		0.36310
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.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Eye disorders	No. of Events (%)	66 (32.4)	19 (9.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.832 (2.300, 6.384)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.58214
Dry eye	No. of Events (%)	14 (6.9)	3 (1.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.640 (1.333, 16.145)
	Treatment P-value [b]		0.00799
	Interaction P-value [c]		0.99028

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Lacrimation increased	No. of Events (%)	27 (13.2)	10 (4.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.705 (1.309, 5.589)
	Treatment P-value [b]		0.00519
	Interaction P-value [c]		0.85675
Vision blurred	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]		4.883 (1.070, 22.277)
	Treatment P-value [b]		0.02355
	Interaction P-value [c]		0.42650

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Diarrhoea	No. of Events (%)	78 (38.2)	52 (25.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.523 (1.072, 2.163)
	Treatment P-value [b]		0.01698
	Interaction P-value [c]		0.98670
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]		5.745 (1.684, 19.604)
	Treatment P-value [b]		0.00158
	Interaction P-value [c]		0.17214

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	15 (7.4)	3 (1.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.963 (1.437, 17.141)
	Treatment P-value [b]		0.00512
	Interaction P-value [c]		0.22773
Fatigue	No. of Events (%)	78 (38.2)	57 (27.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.375 (0.977, 1.935)
	Treatment P-value [b]		0.06659
	Interaction P-value [c]		0.77856

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Pyrexia	No. of Events (%)	49 (24.0)	28 (13.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (29.73, NC)
	Hazard Ratio (95% CI) [a]		1.774 (1.115, 2.822)
	Treatment P-value [b]		0.01403
	Interaction P-value [c]		0.18028
Infections and infestations	No. of Events (%)	110 (53.9)	79 (38.7)
	Median Survival Est. (95% CI)	5.45 (3.45, 21.19)	NC (14.88, NC)
	Hazard Ratio (95% CI) [a]		1.496 (1.120, 1.997)
	Treatment P-value [b]		0.00558
	Interaction P-value [c]		0.93705

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		8.863 (1.123, 69.970)
	Treatment P-value [b]		0.01131
	Interaction P-value [c]		0.62334
Alanine aminotransferase increased	No. of Events (%)	20 (9.8)	5 (2.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.100 (1.539, 10.925)
	Treatment P-value [b]		0.00236
	Interaction P-value [c]		0.79639

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Aspartate aminotransferase increased	No. of Events (%)	27 (13.2)	4 (2.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.078 (2.476, 20.228)
	Treatment P-value [b]		0.00002
	Interaction P-value [c]		0.58540
Blood creatinine increased	No. of Events (%)	21 (10.3)	6 (2.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	30.62 (30.62, NC)
	Hazard Ratio (95% CI) [a]		3.492 (1.409, 8.654)
	Treatment P-value [b]		0.00423
	Interaction P-value [c]		0.91656

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Neutrophil count decreased	No. of Events (%)	21 (10.3)	43 (21.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.426 (0.253, 0.718)
	Treatment P-value [b]		0.00107
	Interaction P-value [c]		0.13208
Weight decreased	No. of Events (%)	36 (17.6)	12 (5.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.141 (1.634, 6.037)
	Treatment P-value [b]		0.00029
	Interaction P-value [c]		0.09334

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
White blood cell count decreased	No. of Events (%)	14 (6.9)	29 (14.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.436 (0.230, 0.825)
	Treatment P-value [b]		0.00935
	Interaction P-value [c]		0.83138
Metabolism and nutrition disorders	No. of Events (%)	121 (59.3)	94 (46.1)
	Median Survival Est. (95% CI)	3.06 (1.84, 5.78)	18.63 (5.29, NC)
	Hazard Ratio (95% CI) [a]		1.326 (1.012, 1.736)
	Treatment P-value [b]		0.03569
	Interaction P-value [c]		0.48971

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Decreased appetite	No. of Events (%)	84 (41.2)	57 (27.9)
	Median Survival Est. (95% CI)	NC (9.56, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.491 (1.065, 2.087)
	Treatment P-value [b]		0.01889
	Interaction P-value [c]		0.93498
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

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Musculoskeletal and connective tissue disorders	No. of Events (%)	79 (38.7)	86 (42.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	28.32 (6.01, NC)
	Hazard Ratio (95% CI) [a]		0.780 (0.575, 1.060)
	Treatment P-value [b]		0.11518
	Interaction P-value [c]		0.35310
Arthralgia	No. of Events (%)	21 (10.3)	32 (15.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.589 (0.340, 1.022)
	Treatment P-value [b]		0.05904
	Interaction P-value [c]		0.61829

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Myalgia	No. of Events (%)	13 (6.4)	24 (11.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.501 (0.255, 0.984)
	Treatment P-value [b]		0.04310
	Interaction P-value [c]		0.17271
Nervous system disorders	No. of Events (%)	144 (70.6)	98 (48.0)
	Median Survival Est. (95% CI)	2.69 (1.87, 3.09)	6.97 (3.94, NC)
	Hazard Ratio (95% CI) [a]		1.636 (1.265, 2.116)
	Treatment P-value [b]		0.00015
	Interaction P-value [c]		0.11038

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Dysgeusia	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]		4.086 (2.351, 7.101)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.14228
Peripheral sensory neuropathy	No. of Events (%)	81 (39.7)	53 (26.0)
	Median Survival Est. (95% CI)	NC (10.58, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.484 (1.050, 2.099)
	Treatment P-value [b]		0.02434
	Interaction P-value [c]		0.88792

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Depression	No. of Events (%)	10 (4.9)	1 (0.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.795 (1.254, 76.530)
	Treatment P-value [b]		0.00746
	Interaction P-value [c]		0.17361
Renal and urinary disorders	No. of Events (%)	64 (31.4)	42 (20.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.541 (1.044, 2.275)
	Treatment P-value [b]		0.02930
	Interaction P-value [c]		0.60470

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	70 (34.3)	53 (26.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.338 (0.936, 1.912)
	Treatment P-value [b]		0.10906
	Interaction P-value [c]		0.69514
Skin and subcutaneous tissue disorders	No. of Events (%)	172 (84.3)	109 (53.4)
	Median Survival Est. (95% CI)	0.66 (0.46, 0.82)	3.12 (0.76, NC)
	Hazard Ratio (95% CI) [a]		2.166 (1.702, 2.758)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.58547

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Drug eruption	No. of Events (%)	18 (8.8)	3 (1.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.078 (1.790, 20.637)
	Treatment P-value [b]		0.00096
	Interaction P-value [c]		0.33916
Dry skin	No. of Events (%)	38 (18.6)	8 (3.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.972 (2.320, 10.658)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.40018

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	71 (34.8)	15 (7.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.629 (3.224, 9.826)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.91188
Rash	No. of Events (%)	42 (20.6)	16 (7.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.783 (1.564, 4.951)
	Treatment P-value [b]		0.00030
	Interaction P-value [c]		0.49566

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		9.026 (1.143, 71.248)
	Treatment P-value [b]		0.01123
	Interaction P-value [c]		0.99460
Rash maculo-papular	No. of Events (%)	34 (16.7)	5 (2.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.083 (2.770, 18.111)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.86307

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Skin hyperpigmentation	No. of Events (%)	17 (8.3)	2 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		8.621 (1.991, 37.321)
	Treatment P-value [b]		0.00054
	Interaction P-value [c]		0.99187

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: 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]		1.180 (0.914, 1.523)
	Treatment P-value [b]		0.22166
	Interaction P-value [c]		0.02894
Blood and lymphatic system disorders	No. of Events (%)	44 (31.4)	29 (27.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.150 (0.720, 1.839)
	Treatment P-value [b]		0.57900
	Interaction P-value [c]		0.00103

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Anaemia	No. of Events (%)	36 (25.7)	19 (17.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.456 (0.835, 2.538)
	Treatment P-value [b]		0.18397
	Interaction P-value [c]		0.00047
Eye disorders	No. of Events (%)	37 (26.4)	8 (7.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.880 (1.807, 8.333)
	Treatment P-value [b]		0.00017
	Interaction P-value [c]		0.05011

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: 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]		8.375 (1.081, 64.874)
	Treatment P-value [b]		0.01385
	Interaction P-value [c]		0.76443
Lacrimation increased	No. of Events (%)	17 (12.1)	1 (0.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		13.071 (1.742, 98.080)
	Treatment P-value [b]		0.00114
	Interaction P-value [c]		0.00520

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Diarrhoea	No. of Events (%)	50 (35.7)	21 (19.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (25.56, NC)
	Hazard Ratio (95% CI) [a]		1.980 (1.189, 3.297)
	Treatment P-value [b]		0.00700
	Interaction P-value [c]		0.00509
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]		10.198 (1.334, 77.956)
	Treatment P-value [b]		0.00555
	Interaction P-value [c]		0.13824

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Chills	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]		2.522 (0.694, 9.168)
	Treatment P-value [b]		0.14298
	Interaction P-value [c]		0.84553
Fatigue	No. of Events (%)	58 (41.4)	38 (35.5)
	Median Survival Est. (95% CI)	NC (6.51, NC)	NC (18.07, NC)
	Hazard Ratio (95% CI) [a]		1.207 (0.802, 1.818)
	Treatment P-value [b]		0.36281
	Interaction P-value [c]		0.30245

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Pyrexia	No. of Events (%)	38 (27.1)	12 (11.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (29.73, NC)
	Hazard Ratio (95% CI) [a]		2.584 (1.350, 4.945)
	Treatment P-value [b]		0.00288
	Interaction P-value [c]		0.00453
Infections and infestations	No. of Events (%)	71 (50.7)	42 (39.3)
	Median Survival Est. (95% CI)	9.03 (3.52, NC)	NC (6.21, NC)
	Hazard Ratio (95% CI) [a]		1.348 (0.920, 1.974)
	Treatment P-value [b]		0.12019
	Interaction P-value [c]		0.75978

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
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]		2.203 (0.229, 21.182)
	Treatment P-value [b]		0.50933
	Interaction P-value [c]		0.75851
Alanine aminotransferase increased	No. of Events (%)	13 (9.3)	3 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.354 (0.956, 11.772)
	Treatment P-value [b]		0.04552
	Interaction P-value [c]		0.89981

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Aspartate aminotransferase increased	No. of Events (%)	18 (12.9)	2 (1.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.163 (1.662, 30.872)
	Treatment P-value [b]		0.00206
	Interaction P-value [c]		0.89823
Blood creatinine increased	No. of Events (%)	11 (7.9)	4 (3.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	30.62 (30.62, NC)
	Hazard Ratio (95% CI) [a]		2.072 (0.659, 6.507)
	Treatment P-value [b]		0.19630
	Interaction P-value [c]		0.38647

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Neutrophil count decreased	No. of Events (%)	17 (12.1)	14 (13.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.877 (0.432, 1.779)
	Treatment P-value [b]		0.68179
	Interaction P-value [c]		0.24618
Weight decreased	No. of Events (%)	24 (17.1)	8 (7.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.385 (1.071, 5.309)
	Treatment P-value [b]		0.02770
	Interaction P-value [c]		0.05357

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
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]		0.520 (0.165, 1.639)
	Treatment P-value [b]		0.26725
	Interaction P-value [c]		0.84307
Metabolism and nutrition disorders	No. of Events (%)	89 (63.6)	34 (31.8)
	Median Survival Est. (95% CI)	2.20 (1.41, 3.94)	NC (25.33, NC)
	Hazard Ratio (95% CI) [a]		2.509 (1.689, 3.726)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.00036

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Decreased appetite	No. of Events (%)	63 (45.0)	19 (17.8)
	Median Survival Est. (95% CI)	NC (4.90, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.880 (1.724, 4.812)
	Treatment P-value [b]		0.00001
	Interaction P-value [c]		0.00340
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

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Musculoskeletal and connective tissue disorders	No. of Events (%)	56 (40.0)	55 (51.4)
	Median Survival Est. (95% CI)	NC (7.59, NC)	5.68 (1.35, NC)
	Hazard Ratio (95% CI) [a]		0.597 (0.411, 0.866)
	Treatment P-value [b]		0.00658
	Interaction P-value [c]		0.63896
Arthralgia	No. of Events (%)	12 (8.6)	22 (20.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.350 (0.173, 0.707)
	Treatment P-value [b]		0.00270
	Interaction P-value [c]		0.11001

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Myalgia	No. of Events (%)	9 (6.4)	18 (16.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.347 (0.156, 0.772)
	Treatment P-value [b]		0.00744
	Interaction P-value [c]		0.91704
Nervous system disorders	No. of Events (%)	89 (63.6)	68 (63.6)
	Median Survival Est. (95% CI)	3.25 (2.46, 4.14)	2.40 (1.15, 3.68)
	Hazard Ratio (95% CI) [a]		0.833 (0.607, 1.142)
	Treatment P-value [b]		0.24686
	Interaction P-value [c]		0.00006

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Dysgeusia	No. of Events (%)	32 (22.9)	3 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		8.828 (2.703, 28.825)
	Treatment P-value [b]		0.00001
	Interaction P-value [c]		0.17989
Peripheral sensory neuropathy	No. of Events (%)	57 (40.7)	42 (39.3)
	Median Survival Est. (95% CI)	NC (5.72, NC)	NC (6.47, NC)
	Hazard Ratio (95% CI) [a]		0.817 (0.548, 1.218)
	Treatment P-value [b]		0.32702
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Renal and urinary disorders	No. of Events (%)	43 (30.7)	19 (17.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (25.26, NC)
	Hazard Ratio (95% CI) [a]		1.804 (1.051, 3.096)
	Treatment P-value [b]		0.02918
	Interaction P-value [c]		0.56504
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	49 (35.0)	35 (32.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.064 (0.689, 1.642)
	Treatment P-value [b]		0.78473
	Interaction P-value [c]		0.24695

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: 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)	72 (67.3)
	Median Survival Est. (95% CI)	0.54 (0.39, 0.82)	0.69 (0.59, 0.95)
	Hazard Ratio (95% CI) [a]		1.404 (1.044, 1.887)
	Treatment P-value [b]		0.02741
	Interaction P-value [c]		0.00367
Drug eruption	No. of Events (%)	17 (12.1)	5 (4.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.618 (0.966, 7.095)
	Treatment P-value [b]		0.04990
	Interaction P-value [c]		0.66005

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Dry skin	No. of Events (%)	23 (16.4)	7 (6.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (26.94, NC)
	Hazard Ratio (95% CI) [a]		2.550 (1.094, 5.943)
	Treatment P-value [b]		0.02805
	Interaction P-value [c]		0.34565
Pruritus	No. of Events (%)	53 (37.9)	12 (11.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.075 (2.177, 7.627)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.38415

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Rash	No. of Events (%)	18 (12.9)	9 (8.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.510 (0.678, 3.362)
	Treatment P-value [b]		0.31044
	Interaction P-value [c]		0.11963
Rash maculo-papular	No. of Events (%)	27 (19.3)	5 (4.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.397 (1.693, 11.420)
	Treatment P-value [b]		0.00098
	Interaction P-value [c]		0.42166

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Paclitaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Skin hyperpigmentation	No. of Events (%)	9 (6.4)	1 (0.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (26.87, NC)
	Hazard Ratio (95% CI) [a]		7.029 (0.890, 55.486)
	Treatment P-value [b]		0.03178
	Interaction P-value [c]		0.94920

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: 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]		0.819 (0.615, 1.090)
	Treatment P-value [b]		0.11081
	Interaction P-value [c]		0.02894
Blood and lymphatic system disorders	No. of Events (%)	22 (25.9)	55 (50.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	7.69 (1.41, NC)
	Hazard Ratio (95% CI) [a]		0.385 (0.235, 0.631)
	Treatment P-value [b]		0.00012
	Interaction P-value [c]		0.00103

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Anaemia	No. of Events (%)	12 (14.1)	39 (35.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (12.94, NC)
	Hazard Ratio (95% CI) [a]		0.321 (0.168, 0.614)
	Treatment P-value [b]		0.00043
	Interaction P-value [c]		0.00047
Eye disorders	No. of Events (%)	24 (28.2)	15 (13.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.066 (1.084, 3.938)
	Treatment P-value [b]		0.02691
	Interaction P-value [c]		0.05011

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: 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]		3.141 (0.609, 16.192)
	Treatment P-value [b]		0.15054
	Interaction P-value [c]		0.76443
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]		0.700 (0.254, 1.928)
	Treatment P-value [b]		0.48268
	Interaction P-value [c]		0.00520

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Docetaxel

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 (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.773 (0.458, 1.303)
	Treatment P-value [b]		0.38500
	Interaction P-value [c]		0.00509
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]		0.940 (0.210, 4.200)
	Treatment P-value [b]		0.91292
	Interaction P-value [c]		0.13824

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: 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]		3.154 (0.612, 16.264)
	Treatment P-value [b]		0.13460
	Interaction P-value [c]		0.84553
Fatigue	No. of Events (%)	33 (38.8)	34 (31.2)
	Median Survival Est. (95% CI)	NC (6.93, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.156 (0.716, 1.866)
	Treatment P-value [b]		0.55576
	Interaction P-value [c]		0.30245

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Pyrexia	No. of Events (%)	14 (16.5)	26 (23.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.629 (0.328, 1.205)
	Treatment P-value [b]		0.15741
	Interaction P-value [c]		0.00453
Infections and infestations	No. of Events (%)	45 (52.9)	37 (33.9)
	Median Survival Est. (95% CI)	5.09 (2.56, NC)	NC (14.88, NC)
	Hazard Ratio (95% CI) [a]		1.675 (1.084, 2.587)
	Treatment P-value [b]		0.02061
	Interaction P-value [c]		0.75978

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
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]		0.75851
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]		5.095 (1.081, 24.004)
	Treatment P-value [b]		0.01807
	Interaction P-value [c]		0.89981

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
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]		4.825 (1.346, 17.295)
	Treatment P-value [b]		0.00694
	Interaction P-value [c]		0.89823
Blood creatinine increased	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]		7.630 (1.706, 34.127)
	Treatment P-value [b]		0.00220
	Interaction P-value [c]		0.38647

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Neutrophil count decreased	No. of Events (%)	13 (15.3)	33 (30.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.396 (0.208, 0.752)
	Treatment P-value [b]		0.00602
	Interaction P-value [c]		0.24618
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]		5.411 (1.808, 16.188)
	Treatment P-value [b]		0.00067
	Interaction P-value [c]		0.05357

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
White blood cell count decreased	No. of Events (%)	10 (11.8)	23 (21.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.477 (0.227, 1.004)
	Treatment P-value [b]		0.05392
	Interaction P-value [c]		0.84307
Metabolism and nutrition disorders	No. of Events (%)	48 (56.5)	53 (48.6)
	Median Survival Est. (95% CI)	1.91 (0.76, NC)	14.92 (1.41, NC)
	Hazard Ratio (95% CI) [a]		1.184 (0.801, 1.750)
	Treatment P-value [b]		0.40575
	Interaction P-value [c]		0.00036

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
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]		1.263 (0.761, 2.095)
	Treatment P-value [b]		0.34367
	Interaction P-value [c]		0.00340
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

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
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]		0.789 (0.469, 1.326)
	Treatment P-value [b]		0.41703
	Interaction P-value [c]		0.63896
Arthralgia	No. of Events (%)	7 (8.2)	9 (8.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.945 (0.352, 2.537)
	Treatment P-value [b]		0.91975
	Interaction P-value [c]		0.11001

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Myalgia	No. of Events (%)	2 (2.4)	8 (7.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.297 (0.063, 1.400)
	Treatment P-value [b]		0.09043
	Interaction P-value [c]		0.91704
Nervous system disorders	No. of Events (%)	60 (70.6)	49 (45.0)
	Median Survival Est. (95% CI)	2.73 (1.31, 3.71)	NC (3.45, NC)
	Hazard Ratio (95% CI) [a]		1.814 (1.243, 2.646)
	Treatment P-value [b]		0.00191
	Interaction P-value [c]		0.00006

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Dysgeusia	No. of Events (%)	29 (34.1)	16 (14.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.508 (1.362, 4.619)
	Treatment P-value [b]		0.00266
	Interaction P-value [c]		0.17989
Peripheral sensory neuropathy	No. of Events (%)	33 (38.8)	23 (21.1)
	Median Survival Est. (95% CI)	NC (5.13, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.859 (1.092, 3.166)
	Treatment P-value [b]		0.02169
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Renal and urinary disorders	No. of Events (%)	20 (23.5)	20 (18.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.247 (0.671, 2.319)
	Treatment P-value [b]		0.46477
	Interaction P-value [c]		0.56504
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	33 (38.8)	23 (21.1)
	Median Survival Est. (95% CI)	NC (6.01, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.911 (1.122, 3.254)
	Treatment P-value [b]		0.01455
	Interaction P-value [c]		0.24695

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: 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)	58 (53.2)
	Median Survival Est. (95% CI)	0.46 (0.36, 0.76)	3.32 (0.95, NC)
	Hazard Ratio (95% CI) [a]		2.536 (1.792, 3.590)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.00367
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]		7.772 (0.935, 64.573)
	Treatment P-value [b]		0.02266
	Interaction P-value [c]		0.66005

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Docetaxel

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]		6.081 (2.057, 17.976)
	Treatment P-value [b]		0.00014
	Interaction P-value [c]		0.34565
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]		6.040 (2.776, 13.145)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.38415

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Rash	No. of Events (%)	16 (18.8)	9 (8.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.378 (1.051, 5.384)
	Treatment P-value [b]		0.03392
	Interaction P-value [c]		0.11963
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]		14.009 (3.274, 59.948)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.42166

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Skin hyperpigmentation	No. of Events (%)	9 (10.6)	1 (0.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		11.375 (1.439, 89.939)
	Treatment P-value [b]		0.00301
	Interaction P-value [c]		0.94920

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
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]		0.695 (0.501, 0.966)
	Treatment P-value [b]		0.04043
	Interaction P-value [c]		0.02894
Blood and lymphatic system disorders	No. of Events (%)	21 (29.6)	44 (58.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	2.66 (1.38, 16.59)
	Hazard Ratio (95% CI) [a]		0.368 (0.219, 0.620)
	Treatment P-value [b]		0.00011
	Interaction P-value [c]		0.00103

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Anaemia	No. of Events (%)	14 (19.7)	33 (44.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	22.97 (3.48, NC)
	Hazard Ratio (95% CI) [a]		0.381 (0.204, 0.713)
	Treatment P-value [b]		0.00125
	Interaction P-value [c]		0.00047
Eye disorders	No. of Events (%)	25 (35.2)	3 (4.0)
	Median Survival Est. (95% CI)	NC (7.39, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		10.848 (3.275, 35.937)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.05011

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Dry eye	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]		0.03812
	Interaction P-value [c]		0.76443
Lacrimation increased	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]		12.583 (1.624, 97.461)
	Treatment P-value [b]		0.00214
	Interaction P-value [c]		0.00520

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Diarrhoea	No. of Events (%)	32 (45.1)	15 (20.0)
	Median Survival Est. (95% CI)	NC (2.40, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.637 (1.428, 4.871)
	Treatment P-value [b]		0.00092
	Interaction P-value [c]		0.00509
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]		4.516 (0.959, 21.270)
	Treatment P-value [b]		0.03966
	Interaction P-value [c]		0.13824

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Chills	No. of Events (%)	5 (7.0)	1 (1.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.283 (0.618, 45.171)
	Treatment P-value [b]		0.09744
	Interaction P-value [c]		0.84553
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]		2.316 (1.048, 5.119)
	Treatment P-value [b]		0.03108
	Interaction P-value [c]		0.30245

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Pyrexia	No. of Events (%)	16 (22.5)	7 (9.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.483 (1.022, 6.037)
	Treatment P-value [b]		0.03823
	Interaction P-value [c]		0.00453
Infections and infestations	No. of Events (%)	41 (57.7)	32 (42.7)
	Median Survival Est. (95% CI)	3.84 (2.17, 11.33)	17.68 (5.36, NC)
	Hazard Ratio (95% CI) [a]		1.518 (0.956, 2.410)
	Treatment P-value [b]		0.07285
	Interaction P-value [c]		0.75978

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Conjunctivitis	No. of Events (%)	11 (15.5)	2 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.178 (1.369, 27.877)
	Treatment P-value [b]		0.00747
	Interaction P-value [c]		0.75851
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]		3.251 (0.656, 16.107)
	Treatment P-value [b]		0.12988
	Interaction P-value [c]		0.89981

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
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]		7.548 (0.929, 61.352)
	Treatment P-value [b]		0.02668
	Interaction P-value [c]		0.89823
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]		2.636 (0.512, 13.589)
	Treatment P-value [b]		0.21910
	Interaction P-value [c]		0.38647

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
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]		0.447 (0.138, 1.451)
	Treatment P-value [b]		0.15172
	Interaction P-value [c]		0.24618
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]		0.918 (0.354, 2.380)
	Treatment P-value [b]		0.83416
	Interaction P-value [c]		0.05357

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
White blood cell count decreased	No. of Events (%)	1 (1.4)	4 (5.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.252 (0.028, 2.255)
	Treatment P-value [b]		0.16926
	Interaction P-value [c]		0.84307
Metabolism and nutrition disorders	No. of Events (%)	39 (54.9)	44 (58.7)
	Median Survival Est. (95% CI)	2.14 (1.31, NC)	2.33 (0.69, 16.59)
	Hazard Ratio (95% CI) [a]		0.788 (0.512, 1.212)
	Treatment P-value [b]		0.30692
	Interaction P-value [c]		0.00036

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Decreased appetite	No. of Events (%)	30 (42.3)	33 (44.0)
	Median Survival Est. (95% CI)	NC (2.79, NC)	NC (2.79, NC)
	Hazard Ratio (95% CI) [a]		0.864 (0.527, 1.416)
	Treatment P-value [b]		0.59401
	Interaction P-value [c]		0.00340
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

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Musculoskeletal and connective tissue disorders	No. of Events (%)	26 (36.6)	33 (44.0)
	Median Survival Est. (95% CI)	NC (6.31, NC)	NC (2.83, NC)
	Hazard Ratio (95% CI) [a]		0.742 (0.444, 1.240)
	Treatment P-value [b]		0.23725
	Interaction P-value [c]		0.63896
Arthralgia	No. of Events (%)	10 (14.1)	10 (13.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.007 (0.419, 2.420)
	Treatment P-value [b]		0.95228
	Interaction P-value [c]		0.11001

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
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]		0.438 (0.135, 1.422)
	Treatment P-value [b]		0.16943
	Interaction P-value [c]		0.91704
Nervous system disorders	No. of Events (%)	43 (60.6)	22 (29.3)
	Median Survival Est. (95% CI)	2.43 (1.87, 3.94)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.873 (1.717, 4.807)
	Treatment P-value [b]		0.00004
	Interaction P-value [c]		0.00006

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
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]		3.261 (1.174, 9.055)
	Treatment P-value [b]		0.01592
	Interaction P-value [c]		0.17989
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]		5.877 (1.701, 20.300)
	Treatment P-value [b]		0.00164
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Renal and urinary disorders	No. of Events (%)	21 (29.6)	18 (24.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.220 (0.650, 2.290)
	Treatment P-value [b]		0.56176
	Interaction P-value [c]		0.56504
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	20 (28.2)	16 (21.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.378 (0.714, 2.660)
	Treatment P-value [b]		0.33914
	Interaction P-value [c]		0.24695

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	53 (74.6)	25 (33.3)
	Median Survival Est. (95% CI)	0.95 (0.62, 1.18)	NC (12.22, NC)
	Hazard Ratio (95% CI) [a]		3.237 (2.010, 5.214)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.00367
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]		0.66005

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Dry skin	No. of Events (%)	12 (16.9)	2 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.736 (1.508, 30.101)
	Treatment P-value [b]		0.00390
	Interaction P-value [c]		0.34565
Pruritus	No. of Events (%)	19 (26.8)	2 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		11.693 (2.726, 50.154)
	Treatment P-value [b]		0.00003
	Interaction P-value [c]		0.38415

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Rash	No. of Events (%)	18 (25.4)	3 (4.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.017 (2.067, 23.822)
	Treatment P-value [b]		0.00026
	Interaction P-value [c]		0.11963
Rash maculo-papular	No. of Events (%)	5 (7.0)	1 (1.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.260 (0.615, 45.013)
	Treatment P-value [b]		0.11070
	Interaction P-value [c]		0.42166

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 hyperpigmentation	No. of Events (%)	2 (2.8)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.13682
	Interaction P-value [c]		0.94920

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Any Event	No. of Events (%)	95 (99.0)	101 (99.0)
	Median Survival Est. (95% CI)	0.20 (0.13, 0.26)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.840 (0.635, 1.113)
	Treatment P-value [b]		0.17896
	Interaction P-value [c]		0.44306
Blood and lymphatic system disorders	No. of Events (%)	31 (32.3)	43 (42.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (5.36, NC)
	Hazard Ratio (95% CI) [a]		0.652 (0.411, 1.035)
	Treatment P-value [b]		0.07518
	Interaction P-value [c]		0.43057

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		0.856 (0.491, 1.493)
	Treatment P-value [b]		0.62423
	Interaction P-value [c]		0.12996
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.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Eye disorders	No. of Events (%)	28 (29.2)	10 (9.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.213 (1.561, 6.615)
	Treatment P-value [b]		0.00085
	Interaction P-value [c]		0.72713
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]		0.98882

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Lacrimation increased	No. of Events (%)	7 (7.3)	3 (2.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.470 (0.639, 9.551)
	Treatment P-value [b]		0.18572
	Interaction P-value [c]		0.87576
Vision blurred	No. of Events (%)	3 (3.1)	3 (2.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.026 (0.207, 5.086)
	Treatment P-value [b]		0.98316
	Interaction P-value [c]		0.09707

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Diarrhoea	No. of Events (%)	31 (32.3)	25 (24.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.328 (0.784, 2.249)
	Treatment P-value [b]		0.28881
	Interaction P-value [c]		0.55092
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]		4.903 (1.059, 22.694)
	Treatment P-value [b]		0.02626
	Interaction P-value [c]		0.57234

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		2.658 (0.516, 13.703)
	Treatment P-value [b]		0.22208
	Interaction P-value [c]		0.78644
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]		1.046 (0.633, 1.728)
	Treatment P-value [b]		0.86786
	Interaction P-value [c]		0.24400

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Pyrexia	No. of Events (%)	21 (21.9)	18 (17.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.195 (0.637, 2.243)
	Treatment P-value [b]		0.58025
	Interaction P-value [c]		0.39408
Infections and infestations	No. of Events (%)	44 (45.8)	34 (33.3)
	Median Survival Est. (95% CI)	21.19 (2.89, NC)	NC (17.97, NC)
	Hazard Ratio (95% CI) [a]		1.427 (0.912, 2.233)
	Treatment P-value [b]		0.13905
	Interaction P-value [c]		0.84794

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		0.04441
	Interaction P-value [c]		0.98984
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]		0.98567

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		11.059 (1.416, 86.339)
	Treatment P-value [b]		0.00432
	Interaction P-value [c]		0.49779
Blood creatinine increased	No. of Events (%)	7 (7.3)	3 (2.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.422 (0.626, 9.375)
	Treatment P-value [b]		0.18281
	Interaction P-value [c]		0.56954

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Neutrophil count decreased	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]		0.691 (0.363, 1.316)
	Treatment P-value [b]		0.26128
	Interaction P-value [c]		0.30802
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]		2.133 (0.861, 5.286)
	Treatment P-value [b]		0.09453
	Interaction P-value [c]		0.83637

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		0.489 (0.183, 1.302)
	Treatment P-value [b]		0.15302
	Interaction P-value [c]		0.72933
Metabolism and nutrition disorders	No. of Events (%)	61 (63.5)	47 (46.1)
	Median Survival Est. (95% CI)	2.04 (1.02, 5.06)	NC (1.45, NC)
	Hazard Ratio (95% CI) [a]		1.424 (0.973, 2.084)
	Treatment P-value [b]		0.07125
	Interaction P-value [c]		0.90619

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Decreased appetite	No. of Events (%)	42 (43.8)	29 (28.4)
	Median Survival Est. (95% CI)	NC (5.06, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.527 (0.951, 2.452)
	Treatment P-value [b]		0.07574
	Interaction P-value [c]		0.93941
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

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Musculoskeletal and connective tissue disorders	No. of Events (%)	31 (32.3)	44 (43.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (4.30, NC)
	Hazard Ratio (95% CI) [a]		0.623 (0.393, 0.986)
	Treatment P-value [b]		0.04411
	Interaction P-value [c]		0.44514
Arthralgia	No. of Events (%)	6 (6.3)	15 (14.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.381 (0.148, 0.982)
	Treatment P-value [b]		0.03891
	Interaction P-value [c]		0.21661

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Myalgia	No. of Events (%)	1 (1.0)	12 (11.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.083 (0.011, 0.639)
	Treatment P-value [b]		0.00167
	Interaction P-value [c]		0.09176
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]		1.500 (1.038, 2.167)
	Treatment P-value [b]		0.02530
	Interaction P-value [c]		0.87312

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Dysgeusia	No. of Events (%)	27 (28.1)	10 (9.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.059 (1.480, 6.320)
	Treatment P-value [b]		0.00126
	Interaction P-value [c]		0.77006
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]		1.579 (0.969, 2.574)
	Treatment P-value [b]		0.06545
	Interaction P-value [c]		0.72505

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Depression	No. of Events (%)	2 (2.1)	1 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.089 (0.189, 23.044)
	Treatment P-value [b]		0.53117
	Interaction P-value [c]		0.39797
Renal and urinary disorders	No. of Events (%)	24 (25.0)	18 (17.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.474 (0.800, 2.715)
	Treatment P-value [b]		0.22009
	Interaction P-value [c]		0.94788

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	30 (31.3)	24 (23.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.351 (0.790, 2.311)
	Treatment P-value [b]		0.27147
	Interaction P-value [c]		0.91281
Skin and subcutaneous tissue disorders	No. of Events (%)	84 (87.5)	63 (61.8)
	Median Survival Est. (95% CI)	0.46 (0.36, 0.72)	0.95 (0.72, 3.45)
	Hazard Ratio (95% CI) [a]		2.083 (1.500, 2.892)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.87485

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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
Drug eruption	No. of Events (%)	9 (9.4)	3 (2.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.194 (0.865, 11.800)
	Treatment P-value [b]		0.06456
	Interaction P-value [c]		0.56142

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Dry skin	No. of Events (%)	17 (17.7)	3 (2.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.367 (1.866, 21.729)
	Treatment P-value [b]		0.00073
	Interaction P-value [c]		0.40699
Pruritus	No. of Events (%)	38 (39.6)	9 (8.8)
	Median Survival Est. (95% CI)	NC (5.55, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.590 (2.702, 11.563)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.99994

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Rash	No. of Events (%)	17 (17.7)	9 (8.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.083 (0.928, 4.672)
	Treatment P-value [b]		0.07317
	Interaction P-value [c]		0.56131
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]		8.211 (2.449, 27.532)
	Treatment P-value [b]		0.00004
	Interaction P-value [c]		0.69751

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		0.98952

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		0.962 (0.787, 1.176)
	Treatment P-value [b]		0.78258
	Interaction P-value [c]		0.44306
Blood and lymphatic system disorders	No. of Events (%)	56 (28.0)	85 (45.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	22.97 (4.76, NC)
	Hazard Ratio (95% CI) [a]		0.518 (0.370, 0.726)
	Treatment P-value [b]		0.00008
	Interaction P-value [c]		0.43057

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Anaemia	No. of Events (%)	39 (19.5)	64 (33.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (22.97, NC)
	Hazard Ratio (95% CI) [a]		0.504 (0.339, 0.752)
	Treatment P-value [b]		0.00044
	Interaction P-value [c]		0.12996
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.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Eye disorders	No. of Events (%)	58 (29.0)	16 (8.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.778 (2.172, 6.571)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.72713
Dry eye	No. of Events (%)	12 (6.0)	3 (1.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.721 (1.050, 13.188)
	Treatment P-value [b]		0.03189
	Interaction P-value [c]		0.98882

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Lacrimation increased	No. of Events (%)	27 (13.5)	9 (4.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.795 (1.314, 5.944)
	Treatment P-value [b]		0.00502
	Interaction P-value [c]		0.87576
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]		6.503 (1.478, 28.610)
	Treatment P-value [b]		0.00410
	Interaction P-value [c]		0.09707

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	75 (37.5)	45 (23.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (25.56, NC)
	Hazard Ratio (95% CI) [a]		1.615 (1.116, 2.338)
	Treatment P-value [b]		0.00984
	Interaction P-value [c]		0.55092
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]		2.889 (1.050, 7.950)
	Treatment P-value [b]		0.03141
	Interaction P-value [c]		0.57234

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Chills	No. of Events (%)	15 (7.5)	4 (2.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.493 (1.159, 10.530)
	Treatment P-value [b]		0.01897
	Interaction P-value [c]		0.78644
Fatigue	No. of Events (%)	79 (39.5)	51 (27.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.506 (1.059, 2.142)
	Treatment P-value [b]		0.02193
	Interaction P-value [c]		0.24400

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Pyrexia	No. of Events (%)	47 (23.5)	27 (14.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (29.73, NC)
	Hazard Ratio (95% CI) [a]		1.683 (1.048, 2.702)
	Treatment P-value [b]		0.02869
	Interaction P-value [c]		0.39408
Infections and infestations	No. of Events (%)	113 (56.5)	77 (40.7)
	Median Survival Est. (95% CI)	3.94 (3.06, 8.67)	NC (7.56, NC)
	Hazard Ratio (95% CI) [a]		1.503 (1.125, 2.009)
	Treatment P-value [b]		0.00494
	Interaction P-value [c]		0.84794

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Conjunctivitis	No. of Events (%)	15 (7.5)	3 (1.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.668 (1.351, 16.131)
	Treatment P-value [b]		0.00688
	Interaction P-value [c]		0.98984
Alanine aminotransferase increased	No. of Events (%)	19 (9.5)	7 (3.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.551 (1.072, 6.073)
	Treatment P-value [b]		0.02994
	Interaction P-value [c]		0.98567

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Aspartate aminotransferase increased	No. of Events (%)	26 (13.0)	5 (2.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.048 (1.938, 13.148)
	Treatment P-value [b]		0.00022
	Interaction P-value [c]		0.49779
Blood creatinine increased	No. of Events (%)	21 (10.5)	5 (2.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	30.62 (30.62, NC)
	Hazard Ratio (95% CI) [a]		3.930 (1.481, 10.430)
	Treatment P-value [b]		0.00270
	Interaction P-value [c]		0.56954

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Neutrophil count decreased	No. of Events (%)	18 (9.0)	34 (18.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.442 (0.249, 0.782)
	Treatment P-value [b]		0.00427
	Interaction P-value [c]		0.30802
Weight decreased	No. of Events (%)	34 (17.0)	14 (7.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.396 (1.286, 4.464)
	Treatment P-value [b]		0.00441
	Interaction P-value [c]		0.83637

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
White blood cell count decreased	No. of Events (%)	10 (5.0)	22 (11.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.393 (0.186, 0.830)
	Treatment P-value [b]		0.01108
	Interaction P-value [c]		0.72933
Metabolism and nutrition disorders	No. of Events (%)	115 (57.5)	84 (44.4)
	Median Survival Est. (95% CI)	2.53 (1.41, 6.67)	25.33 (5.68, NC)
	Hazard Ratio (95% CI) [a]		1.384 (1.044, 1.834)
	Treatment P-value [b]		0.02477
	Interaction P-value [c]		0.90619

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Decreased appetite	No. of Events (%)	81 (40.5)	53 (28.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.493 (1.056, 2.111)
	Treatment P-value [b]		0.02337
	Interaction P-value [c]		0.93941
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

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Musculoskeletal and connective tissue disorders	No. of Events (%)	75 (37.5)	79 (41.8)
	Median Survival Est. (95% CI)	NC (13.93, NC)	28.32 (6.01, NC)
	Hazard Ratio (95% CI) [a]		0.774 (0.564, 1.062)
	Treatment P-value [b]		0.11127
	Interaction P-value [c]		0.44514
Arthralgia	No. of Events (%)	23 (11.5)	26 (13.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.762 (0.435, 1.336)
	Treatment P-value [b]		0.33628
	Interaction P-value [c]		0.21661

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		0.526 (0.271, 1.023)
	Treatment P-value [b]		0.06554
	Interaction P-value [c]		0.09176
Nervous system disorders	No. of Events (%)	126 (63.0)	89 (47.1)
	Median Survival Est. (95% CI)	2.99 (2.07, 4.07)	6.97 (3.94, NC)
	Hazard Ratio (95% CI) [a]		1.445 (1.101, 1.896)
	Treatment P-value [b]		0.00860
	Interaction P-value [c]		0.87312

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		3.518 (1.940, 6.382)
	Treatment P-value [b]		0.00001
	Interaction P-value [c]		0.77006
Peripheral sensory neuropathy	No. of Events (%)	65 (32.5)	41 (21.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.411 (0.955, 2.087)
	Treatment P-value [b]		0.08389
	Interaction P-value [c]		0.72505

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Depression	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]		8.189 (1.037, 64.677)
	Treatment P-value [b]		0.01820
	Interaction P-value [c]		0.39797
Renal and urinary disorders	No. of Events (%)	60 (30.0)	39 (20.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (25.26, NC)
	Hazard Ratio (95% CI) [a]		1.438 (0.961, 2.153)
	Treatment P-value [b]		0.06981
	Interaction P-value [c]		0.94788

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	72 (36.0)	50 (26.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.401 (0.976, 2.009)
	Treatment P-value [b]		0.06489
	Interaction P-value [c]		0.91281
Skin and subcutaneous tissue disorders	No. of Events (%)	154 (77.0)	92 (48.7)
	Median Survival Est. (95% CI)	0.79 (0.53, 0.95)	4.21 (2.04, NC)
	Hazard Ratio (95% CI) [a]		2.154 (1.662, 2.791)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.87485

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		8.165 (1.034, 64.462)
	Treatment P-value [b]		0.01741
	Interaction P-value [c]		0.99941
Drug eruption	No. of Events (%)	17 (8.5)	3 (1.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.433 (1.592, 18.544)
	Treatment P-value [b]		0.00245
	Interaction P-value [c]		0.56142

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Dry skin	No. of Events (%)	36 (18.0)	10 (5.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (26.94, NC)
	Hazard Ratio (95% CI) [a]		3.502 (1.737, 7.059)
	Treatment P-value [b]		0.00018
	Interaction P-value [c]		0.40699
Pruritus	No. of Events (%)	65 (32.5)	13 (6.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.589 (3.081, 10.141)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.99994

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Rash	No. of Events (%)	35 (17.5)	12 (6.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.835 (1.471, 5.464)
	Treatment P-value [b]		0.00114
	Interaction P-value [c]		0.56131
Rash maculo-papular	No. of Events (%)	31 (15.5)	5 (2.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.057 (2.355, 15.578)
	Treatment P-value [b]		0.00002
	Interaction P-value [c]		0.69751

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Skin hyperpigmentation	No. of Events (%)	13 (6.5)	2 (1.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (26.87, NC)
	Hazard Ratio (95% CI) [a]		6.085 (1.372, 26.989)
	Treatment P-value [b]		0.00767
	Interaction P-value [c]		0.98952

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Any Event	No. of Events (%)	253 (97.7)	252 (98.8)
	Median Survival Est. (95% CI)	0.16 (0.16, 0.23)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.941 (0.790, 1.121)
	Treatment P-value [b]		0.52328
	Interaction P-value [c]		0.43778
Blood and lymphatic system disorders	No. of Events (%)	80 (30.9)	114 (44.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	22.97 (5.55, NC)
	Hazard Ratio (95% CI) [a]		0.578 (0.434, 0.770)
	Treatment P-value [b]		0.00013
	Interaction P-value [c]		0.48314

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Anaemia	No. of Events (%)	57 (22.0)	79 (31.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.644 (0.458, 0.906)
	Treatment P-value [b]		0.01047
	Interaction P-value [c]		0.26818
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.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Eye disorders	No. of Events (%)	80 (30.9)	22 (8.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.995 (2.492, 6.405)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.13370
Dry eye	No. of Events (%)	19 (7.3)	2 (0.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.378 (2.184, 40.268)
	Treatment P-value [b]		0.00023
	Interaction P-value [c]		0.15014

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Lacrimation increased	No. of Events (%)	34 (13.1)	11 (4.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.056 (1.548, 6.033)
	Treatment P-value [b]		0.00071
	Interaction P-value [c]		0.98319
Vision blurred	No. of Events (%)	15 (5.8)	5 (2.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.896 (1.052, 7.969)
	Treatment P-value [b]		0.03092
	Interaction P-value [c]		0.98948

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Diarrhoea	No. of Events (%)	95 (36.7)	65 (25.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.468 (1.071, 2.014)
	Treatment P-value [b]		0.01726
	Interaction P-value [c]		0.48361
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]		3.694 (1.498, 9.111)
	Treatment P-value [b]		0.00242
	Interaction P-value [c]		0.62717

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Chills	No. of Events (%)	18 (6.9)	6 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.919 (1.158, 7.357)
	Treatment P-value [b]		0.01749
	Interaction P-value [c]		0.98859
Fatigue	No. of Events (%)	97 (37.5)	73 (28.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.305 (0.963, 1.768)
	Treatment P-value [b]		0.08492
	Interaction P-value [c]		0.62500

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Gait disturbance	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]		0.00235
	Interaction P-value [c]		0.99815
Pyrexia	No. of Events (%)	59 (22.8)	43 (16.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (29.73, NC)
	Hazard Ratio (95% CI) [a]		1.334 (0.901, 1.977)
	Treatment P-value [b]		0.14596
	Interaction P-value [c]		0.10821

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Infections and infestations	No. of Events (%)	136 (52.5)	96 (37.6)
	Median Survival Est. (95% CI)	5.45 (3.45, 21.19)	NC (17.68, NC)
	Hazard Ratio (95% CI) [a]		1.481 (1.140, 1.923)
	Treatment P-value [b]		0.00303
	Interaction P-value [c]		0.91631
Conjunctivitis	No. of Events (%)	15 (5.8)	3 (1.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.845 (1.402, 16.743)
	Treatment P-value [b]		0.00554
	Interaction P-value [c]		0.99033

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Alanine aminotransferase increased	No. of Events (%)	21 (8.1)	6 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.426 (1.382, 8.492)
	Treatment P-value [b]		0.00489
	Interaction P-value [c]		0.58152
Aspartate aminotransferase increased	No. of Events (%)	31 (12.0)	5 (2.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.278 (2.441, 16.147)
	Treatment P-value [b]		0.00001
	Interaction P-value [c]		0.86951

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Blood creatinine increased	No. of Events (%)	26 (10.0)	8 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (30.62, NC)
	Hazard Ratio (95% CI) [a]		3.141 (1.420, 6.948)
	Treatment P-value [b]		0.00283
	Interaction P-value [c]		0.98705
Neutrophil count decreased	No. of Events (%)	25 (9.7)	50 (19.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.431 (0.266, 0.696)
	Treatment P-value [b]		0.00041
	Interaction P-value [c]		0.04035

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Weight decreased	No. of Events (%)	43 (16.6)	21 (8.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.062 (1.223, 3.474)
	Treatment P-value [b]		0.00548
	Interaction P-value [c]		0.98003
White blood cell count decreased	No. of Events (%)	10 (3.9)	31 (12.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.289 (0.142, 0.589)
	Treatment P-value [b]		0.00030
	Interaction P-value [c]		0.01831

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Metabolism and nutrition disorders	No. of Events (%)	157 (60.6)	112 (43.9)
	Median Survival Est. (95% CI)	2.14 (1.41, 4.11)	25.33 (6.21, NC)
	Hazard Ratio (95% CI) [a]		1.487 (1.167, 1.896)
	Treatment P-value [b]		0.00121
	Interaction P-value [c]		0.13565
Decreased appetite	No. of Events (%)	108 (41.7)	70 (27.5)
	Median Survival Est. (95% CI)	NC (9.56, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.547 (1.145, 2.091)
	Treatment P-value [b]		0.00402
	Interaction P-value [c]		0.60661

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	92 (35.5)	108 (42.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	28.32 (8.02, NC)
	Hazard Ratio (95% CI) [a]		0.705 (0.534, 0.932)
	Treatment P-value [b]		0.01386
	Interaction P-value [c]		0.63749

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Arthralgia	No. of Events (%)	26 (10.0)	35 (13.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.662 (0.399, 1.101)
	Treatment P-value [b]		0.11029
	Interaction P-value [c]		0.59790
Myalgia	No. of Events (%)	14 (5.4)	31 (12.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.412 (0.219, 0.774)
	Treatment P-value [b]		0.00438
	Interaction P-value [c]		0.59661

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Nervous system disorders	No. of Events (%)	166 (64.1)	121 (47.5)
	Median Survival Est. (95% CI)	2.83 (2.14, 3.71)	6.93 (3.94, NC)
	Hazard Ratio (95% CI) [a]		1.453 (1.149, 1.837)
	Treatment P-value [b]		0.00163
	Interaction P-value [c]		0.90793
Dysgeusia	No. of Events (%)	66 (25.5)	20 (7.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.511 (2.129, 5.791)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.53547

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Peripheral motor neuropathy	No. of Events (%)	12 (4.6)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00129
	Interaction P-value [c]		0.99991
Peripheral sensory neuropathy	No. of Events (%)	90 (34.7)	59 (23.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.432 (1.031, 1.989)
	Treatment P-value [b]		0.03123
	Interaction P-value [c]		0.76834

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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
Depression	No. of Events (%)	11 (4.2)	2 (0.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.281 (1.170, 23.836)
	Treatment P-value [b]		0.01541
	Interaction P-value [c]		0.99960

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Renal and urinary disorders	No. of Events (%)	77 (29.7)	49 (19.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.561 (1.091, 2.233)
	Treatment P-value [b]		0.01399
	Interaction P-value [c]		0.26700
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	91 (35.1)	67 (26.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.371 (1.000, 1.879)
	Treatment P-value [b]		0.05003
	Interaction P-value [c]		0.76842

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Skin and subcutaneous tissue disorders	No. of Events (%)	211 (81.5)	134 (52.5)
	Median Survival Est. (95% CI)	0.62 (0.46, 0.79)	2.86 (1.41, NC)
	Hazard Ratio (95% CI) [a]		2.187 (1.759, 2.720)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.23618
Drug eruption	No. of Events (%)	24 (9.3)	3 (1.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		8.002 (2.409, 26.576)
	Treatment P-value [b]		0.00005
	Interaction P-value [c]		0.02077

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Dry skin	No. of Events (%)	50 (19.3)	13 (5.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.950 (2.145, 7.274)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.98316
Pruritus	No. of Events (%)	92 (35.5)	19 (7.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.717 (3.488, 9.372)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.69820

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Rash	No. of Events (%)	47 (18.1)	17 (6.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.815 (1.616, 4.903)
	Treatment P-value [b]		0.00014
	Interaction P-value [c]		0.25764
Rash maculo-papular	No. of Events (%)	46 (17.8)	8 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.960 (2.812, 12.629)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.98386

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Skin hyperpigmentation	No. of Events (%)	18 (6.9)	2 (0.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (26.87, NC)
	Hazard Ratio (95% CI) [a]		8.814 (2.043, 38.026)
	Treatment P-value [b]		0.00042
	Interaction P-value [c]		0.99061

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Any Event	No. of Events (%)	37 (100.0)	36 (100.0)
	Median Survival Est. (95% CI)	0.23 (0.13, 0.26)	0.13 (0.07, 0.16)
	Hazard Ratio (95% CI) [a]		0.774 (0.489, 1.226)
	Treatment P-value [b]		0.14344
	Interaction P-value [c]		0.43778
Blood and lymphatic system disorders	No. of Events (%)	7 (18.9)	14 (38.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (2.14, NC)
	Hazard Ratio (95% CI) [a]		0.411 (0.166, 1.019)
	Treatment P-value [b]		0.05879
	Interaction P-value [c]		0.48314

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		0.346 (0.122, 0.983)
	Treatment P-value [b]		0.04479
	Interaction P-value [c]		0.26818
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.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		1.422 (0.401, 5.038)
	Treatment P-value [b]		0.57291
	Interaction P-value [c]		0.13370
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]		0.941 (0.059, 15.046)
	Treatment P-value [b]		0.92175
	Interaction P-value [c]		0.15014

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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]		0.98319
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]		0.98948

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		2.178 (0.757, 6.270)
	Treatment P-value [b]		0.14161
	Interaction P-value [c]		0.48361
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]		1.957 (0.177, 21.578)
	Treatment P-value [b]		0.55223
	Interaction P-value [c]		0.62717

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		0.98859
Fatigue	No. of Events (%)	13 (35.1)	8 (22.2)
	Median Survival Est. (95% CI)	NC (4.40, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.646 (0.682, 3.971)
	Treatment P-value [b]		0.26514
	Interaction P-value [c]		0.62500

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Gait disturbance	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]		0.99815
Pyrexia	No. of Events (%)	9 (24.3)	2 (5.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.879 (1.054, 22.587)
	Treatment P-value [b]		0.03241
	Interaction P-value [c]		0.10821

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		1.538 (0.793, 2.985)
	Treatment P-value [b]		0.23191
	Interaction P-value [c]		0.91631
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]		0.04474
	Interaction P-value [c]		0.99033

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		6.550 (0.788, 54.466)
	Treatment P-value [b]		0.04980
	Interaction P-value [c]		0.58152
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]		5.158 (0.603, 44.148)
	Treatment P-value [b]		0.09368
	Interaction P-value [c]		0.86951

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		0.17924
	Interaction P-value [c]		0.98705
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, 3.984)
	Treatment P-value [b]		0.52070
	Interaction P-value [c]		0.04035

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		0.98003
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]		1.885 (0.471, 7.539)
	Treatment P-value [b]		0.35367
	Interaction P-value [c]		0.01831

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		0.886 (0.469, 1.673)
	Treatment P-value [b]		0.74820
	Interaction P-value [c]		0.13565
Decreased appetite	No. of Events (%)	15 (40.5)	12 (33.3)
	Median Survival Est. (95% CI)	NC (1.71, NC)	NC (12.22, NC)
	Hazard Ratio (95% CI) [a]		1.249 (0.584, 2.668)
	Treatment P-value [b]		0.60316
	Interaction P-value [c]		0.60661

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		0.851 (0.411, 1.763)
	Treatment P-value [b]		0.69280
	Interaction P-value [c]		0.63749

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Arthralgia	No. of Events (%)	3 (8.1)	6 (16.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.445 (0.111, 1.781)
	Treatment P-value [b]		0.24898
	Interaction P-value [c]		0.59790
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]		0.222 (0.025, 1.991)
	Treatment P-value [b]		0.15311
	Interaction P-value [c]		0.59661

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Nervous system disorders	No. of Events (%)	26 (70.3)	18 (50.0)
	Median Survival Est. (95% CI)	3.06 (1.25, 4.14)	6.47 (2.27, NC)
	Hazard Ratio (95% CI) [a]		1.510 (0.828, 2.754)
	Treatment P-value [b]		0.19149
	Interaction P-value [c]		0.90793
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]		2.343 (0.721, 7.608)
	Treatment P-value [b]		0.15224
	Interaction P-value [c]		0.53547

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		0.99991
Peripheral sensory neuropathy	No. of Events (%)	15 (40.5)	9 (25.0)
	Median Survival Est. (95% CI)	NC (4.17, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.637 (0.716, 3.741)
	Treatment P-value [b]		0.26762
	Interaction P-value [c]		0.76834

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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
Depression	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]		0.99960

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Renal and urinary disorders	No. of Events (%)	7 (18.9)	8 (22.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (13.83, NC)
	Hazard Ratio (95% CI) [a]		0.849 (0.308, 2.341)
	Treatment P-value [b]		0.71602
	Interaction P-value [c]		0.26700
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]		1.592 (0.617, 4.108)
	Treatment P-value [b]		0.33037
	Interaction P-value [c]		0.76842

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)	21 (58.3)
	Median Survival Est. (95% CI)	0.69 (0.30, 1.18)	2.10 (0.46, NC)
	Hazard Ratio (95% CI) [a]		1.513 (0.855, 2.676)
	Treatment P-value [b]		0.19936
	Interaction P-value [c]		0.23618
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]		0.630 (0.105, 3.771)
	Treatment P-value [b]		0.62284
	Interaction P-value [c]		0.02077

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		0.98316
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]		4.361 (1.216, 15.633)
	Treatment P-value [b]		0.01654
	Interaction P-value [c]		0.69820

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Rash	No. of Events (%)	5 (13.5)	4 (11.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.234 (0.331, 4.598)
	Treatment P-value [b]		0.74541
	Interaction P-value [c]		0.25764
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]		0.98386

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 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]		0.99061

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: 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 (0.07, 0.20)
	Hazard Ratio (95% CI) [a]		1.060 (0.723, 1.554)
	Treatment P-value [b]		0.86274
	Interaction P-value [c]		0.49024
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]		0.344 (0.181, 0.653)
	Treatment P-value [b]		0.00137
	Interaction P-value [c]		0.04646

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: 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]		0.384 (0.176, 0.839)
	Treatment P-value [b]		0.02090
	Interaction P-value [c]		0.12695
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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Eye disorders	No. of Events (%)	17 (27.9)	2 (4.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.379 (1.705, 31.938)
	Treatment P-value [b]		0.00178
	Interaction P-value [c]		0.32792
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]		0.99001

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Lacrimation increased	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]		0.05914
	Interaction P-value [c]		0.98873
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]		0.374 (0.034, 4.124)
	Treatment P-value [b]		0.42697
	Interaction P-value [c]		0.03730

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: 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]		1.113 (0.517, 2.399)
	Treatment P-value [b]		0.76554
	Interaction P-value [c]		0.43160
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]		1.068 (0.239, 4.772)
	Treatment P-value [b]		0.93437
	Interaction P-value [c]		0.04336

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Chills	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]		0.23015
	Interaction P-value [c]		0.99149
Fatigue	No. of Events (%)	22 (36.1)	20 (40.8)
	Median Survival Est. (95% CI)	NC (8.67, NC)	NC (2.10, NC)
	Hazard Ratio (95% CI) [a]		0.806 (0.440, 1.477)
	Treatment P-value [b]		0.49916
	Interaction P-value [c]		0.07841

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Pyrexia	No. of Events (%)	11 (18.0)	10 (20.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.822 (0.349, 1.937)
	Treatment P-value [b]		0.65199
	Interaction P-value [c]		0.06351
Infections and infestations	No. of Events (%)	36 (59.0)	20 (40.8)
	Median Survival Est. (95% CI)	3.15 (2.20, NC)	NC (2.92, NC)
	Hazard Ratio (95% CI) [a]		1.560 (0.903, 2.695)
	Treatment P-value [b]		0.10783
	Interaction P-value [c]		0.95486

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
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]		0.99193
Alanine aminotransferase increased	No. of Events (%)	6 (9.8)	2 (4.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.453 (0.495, 12.156)
	Treatment P-value [b]		0.26371
	Interaction P-value [c]		0.83772

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Aspartate aminotransferase increased	No. of Events (%)	8 (13.1)	2 (4.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.304 (0.702, 15.561)
	Treatment P-value [b]		0.11335
	Interaction P-value [c]		0.29871
Blood creatinine increased	No. of Events (%)	2 (3.3)	1 (2.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.556 (0.141, 17.163)
	Treatment P-value [b]		0.77090
	Interaction P-value [c]		0.46139

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Neutrophil count decreased	No. of Events (%)	8 (13.1)	8 (16.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.740 (0.278, 1.971)
	Treatment P-value [b]		0.51355
	Interaction P-value [c]		0.44663
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]		1.858 (0.480, 7.184)
	Treatment P-value [b]		0.37272
	Interaction P-value [c]		0.63507

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
White blood cell count decreased	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]		0.575 (0.129, 2.571)
	Treatment P-value [b]		0.44679
	Interaction P-value [c]		0.63436
Metabolism and nutrition disorders	No. of Events (%)	37 (60.7)	25 (51.0)
	Median Survival Est. (95% CI)	2.53 (0.62, NC)	18.63 (0.82, NC)
	Hazard Ratio (95% CI) [a]		1.234 (0.743, 2.049)
	Treatment P-value [b]		0.45639
	Interaction P-value [c]		0.82778

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Decreased appetite	No. of Events (%)	31 (50.8)	17 (34.7)
	Median Survival Est. (95% CI)	9.13 (1.77, NC)	NC (12.22, NC)
	Hazard Ratio (95% CI) [a]		1.558 (0.862, 2.816)
	Treatment P-value [b]		0.16588
	Interaction P-value [c]		0.76108
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

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Musculoskeletal and connective tissue disorders	No. of Events (%)	27 (44.3)	20 (40.8)
	Median Survival Est. (95% CI)	13.93 (5.78, NC)	NC (2.83, NC)
	Hazard Ratio (95% CI) [a]		0.988 (0.554, 1.761)
	Treatment P-value [b]		0.90976
	Interaction P-value [c]		0.42161
Arthralgia	No. of Events (%)	7 (11.5)	10 (20.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.488 (0.186, 1.282)
	Treatment P-value [b]		0.14584
	Interaction P-value [c]		0.45228

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
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]		0.568 (0.127, 2.538)
	Treatment P-value [b]		0.47394
	Interaction P-value [c]		0.69825
Nervous system disorders	No. of Events (%)	45 (73.8)	24 (49.0)
	Median Survival Est. (95% CI)	2.73 (1.51, 3.42)	6.97 (1.84, NC)
	Hazard Ratio (95% CI) [a]		1.671 (1.018, 2.744)
	Treatment P-value [b]		0.03608
	Interaction P-value [c]		0.59462

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
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]		2.831 (1.037, 7.729)
	Treatment P-value [b]		0.03474
	Interaction P-value [c]		0.90417
Peripheral sensory neuropathy	No. of Events (%)	25 (41.0)	9 (18.4)
	Median Survival Est. (95% CI)	NC (5.29, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.262 (1.056, 4.846)
	Treatment P-value [b]		0.03352
	Interaction P-value [c]		0.19005

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Depression	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]		0.37724
	Interaction P-value [c]		0.99453
Renal and urinary disorders	No. of Events (%)	17 (27.9)	11 (22.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.213 (0.568, 2.591)
	Treatment P-value [b]		0.62323
	Interaction P-value [c]		0.60324

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	25 (41.0)	10 (20.4)
	Median Survival Est. (95% CI)	NC (4.83, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.141 (1.028, 4.458)
	Treatment P-value [b]		0.03461
	Interaction P-value [c]		0.35429
Skin and subcutaneous tissue disorders	No. of Events (%)	52 (85.2)	26 (53.1)
	Median Survival Est. (95% CI)	0.36 (0.33, 0.53)	2.86 (0.66, NC)
	Hazard Ratio (95% CI) [a]		2.765 (1.723, 4.437)
	Treatment P-value [b]		0.00005
	Interaction P-value [c]		0.27968

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Drug eruption	No. of Events (%)	10 (16.4)	3 (6.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.811 (0.773, 10.217)
	Treatment P-value [b]		0.10112
	Interaction P-value [c]		0.52671
Dry skin	No. of Events (%)	12 (19.7)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00160
	Interaction P-value [c]		0.98609

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
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]		20.560 (2.765, 152.860)
	Treatment P-value [b]		0.00003
	Interaction P-value [c]		0.21843
Rash	No. of Events (%)	14 (23.0)	5 (10.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.380 (0.857, 6.610)
	Treatment P-value [b]		0.08499
	Interaction P-value [c]		0.88476

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
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]		0.99329
Rash maculo-papular	No. of Events (%)	10 (16.4)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00463
	Interaction P-value [c]		0.98782

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
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]		0.99379

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Any Event	No. of Events (%)	197 (97.5)	201 (99.5)
	Median Survival Est. (95% CI)	0.16 (0.16, 0.23)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.911 (0.748, 1.110)
	Treatment P-value [b]		0.32188
	Interaction P-value [c]		0.49024
Blood and lymphatic system disorders	No. of Events (%)	64 (31.7)	80 (39.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (12.94, NC)
	Hazard Ratio (95% CI) [a]		0.715 (0.515, 0.994)
	Treatment P-value [b]		0.03941
	Interaction P-value [c]		0.04646

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Anaemia	No. of Events (%)	46 (22.8)	57 (28.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.758 (0.514, 1.118)
	Treatment P-value [b]		0.14478
	Interaction P-value [c]		0.12695
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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Eye disorders	No. of Events (%)	61 (30.2)	20 (9.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.405 (2.054, 5.642)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.32792
Dry eye	No. of Events (%)	17 (8.4)	3 (1.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.697 (1.669, 19.442)
	Treatment P-value [b]		0.00169
	Interaction P-value [c]		0.99001

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Lacrimation increased	No. of Events (%)	25 (12.4)	9 (4.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.824 (1.318, 6.051)
	Treatment P-value [b]		0.00508
	Interaction P-value [c]		0.98873
Vision blurred	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]		7.462 (1.706, 32.631)
	Treatment P-value [b]		0.00172
	Interaction P-value [c]		0.03730

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Diarrhoea	No. of Events (%)	72 (35.6)	48 (23.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.566 (1.086, 2.257)
	Treatment P-value [b]		0.01508
	Interaction P-value [c]		0.43160
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]		9.222 (2.140, 39.746)
	Treatment P-value [b]		0.00029
	Interaction P-value [c]		0.04336

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Chills	No. of Events (%)	17 (8.4)	6 (3.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.833 (1.117, 7.187)
	Treatment P-value [b]		0.02129
	Interaction P-value [c]		0.99149
Fatigue	No. of Events (%)	77 (38.1)	52 (25.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.512 (1.063, 2.149)
	Treatment P-value [b]		0.01889
	Interaction P-value [c]		0.07841

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Pyrexia	No. of Events (%)	53 (26.2)	27 (13.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (29.73, NC)
	Hazard Ratio (95% CI) [a]		2.068 (1.301, 3.288)
	Treatment P-value [b]		0.00172
	Interaction P-value [c]		0.06351
Infections and infestations	No. of Events (%)	109 (54.0)	78 (38.6)
	Median Survival Est. (95% CI)	4.76 (3.09, 9.66)	NC (10.41, NC)
	Hazard Ratio (95% CI) [a]		1.532 (1.145, 2.050)
	Treatment P-value [b]		0.00395
	Interaction P-value [c]		0.95486

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Conjunctivitis	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]		4.308 (1.227, 15.122)
	Treatment P-value [b]		0.01361
	Interaction P-value [c]		0.99193
Alanine aminotransferase increased	No. of Events (%)	15 (7.4)	5 (2.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.990 (1.086, 8.229)
	Treatment P-value [b]		0.02533
	Interaction P-value [c]		0.83772

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
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]		10.193 (2.382, 43.606)
	Treatment P-value [b]		0.00010
	Interaction P-value [c]		0.29871
Blood creatinine increased	No. of Events (%)	20 (9.9)	5 (2.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (30.62, NC)
	Hazard Ratio (95% CI) [a]		4.123 (1.547, 10.987)
	Treatment P-value [b]		0.00202
	Interaction P-value [c]		0.46139

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Neutrophil count decreased	No. of Events (%)	21 (10.4)	39 (19.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.480 (0.282, 0.816)
	Treatment P-value [b]		0.00630
	Interaction P-value [c]		0.44663
Weight decreased	No. of Events (%)	38 (18.8)	15 (7.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.657 (1.462, 4.831)
	Treatment P-value [b]		0.00084
	Interaction P-value [c]		0.63507

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
White blood cell count decreased	No. of Events (%)	11 (5.4)	26 (12.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.385 (0.190, 0.779)
	Treatment P-value [b]		0.00669
	Interaction P-value [c]		0.63436
Metabolism and nutrition disorders	No. of Events (%)	118 (58.4)	92 (45.5)
	Median Survival Est. (95% CI)	2.20 (1.71, 5.39)	25.33 (5.29, NC)
	Hazard Ratio (95% CI) [a]		1.315 (1.001, 1.728)
	Treatment P-value [b]		0.04581
	Interaction P-value [c]		0.82778

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Decreased appetite	No. of Events (%)	82 (40.6)	58 (28.7)
	Median Survival Est. (95% CI)	NC (9.10, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.402 (1.002, 1.963)
	Treatment P-value [b]		0.04543
	Interaction P-value [c]		0.76108
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

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Musculoskeletal and connective tissue disorders	No. of Events (%)	71 (35.1)	82 (40.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	28.32 (14.85, NC)
	Hazard Ratio (95% CI) [a]		0.754 (0.548, 1.036)
	Treatment P-value [b]		0.08918
	Interaction P-value [c]		0.42161
Arthralgia	No. of Events (%)	22 (10.9)	27 (13.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.749 (0.426, 1.315)
	Treatment P-value [b]		0.31279
	Interaction P-value [c]		0.45228

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Myalgia	No. of Events (%)	10 (5.0)	23 (11.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.408 (0.194, 0.858)
	Treatment P-value [b]		0.01465
	Interaction P-value [c]		0.69825
Nervous system disorders	No. of Events (%)	127 (62.9)	95 (47.0)
	Median Survival Est. (95% CI)	2.96 (2.07, 3.81)	7.66 (3.48, NC)
	Hazard Ratio (95% CI) [a]		1.435 (1.099, 1.872)
	Treatment P-value [b]		0.00773
	Interaction P-value [c]		0.59462

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Dysgeusia	No. of Events (%)	51 (25.2)	18 (8.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.036 (1.774, 5.197)
	Treatment P-value [b]		0.00002
	Interaction P-value [c]		0.90417
Peripheral sensory neuropathy	No. of Events (%)	67 (33.2)	49 (24.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.284 (0.888, 1.856)
	Treatment P-value [b]		0.18136
	Interaction P-value [c]		0.19005

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Depression	No. of Events (%)	8 (4.0)	2 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.886 (0.825, 18.311)
	Treatment P-value [b]		0.06566
	Interaction P-value [c]		0.99453
Renal and urinary disorders	No. of Events (%)	60 (29.7)	40 (19.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.523 (1.021, 2.273)
	Treatment P-value [b]		0.03767
	Interaction P-value [c]		0.60324

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Respiratory, thoracic and mediastinal disorders	No. of Events (%)	69 (34.2)	50 (24.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.454 (1.010, 2.092)
	Treatment P-value [b]		0.04388
	Interaction P-value [c]		0.35429
Skin and subcutaneous tissue disorders	No. of Events (%)	159 (78.7)	105 (52.0)
	Median Survival Est. (95% CI)	0.69 (0.49, 0.89)	3.25 (1.45, NC)
	Hazard Ratio (95% CI) [a]		2.062 (1.610, 2.641)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.27968

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Drug eruption	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]		5.010 (1.451, 17.301)
	Treatment P-value [b]		0.00468
	Interaction P-value [c]		0.52671
Dry skin	No. of Events (%)	37 (18.3)	10 (5.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.926 (1.952, 7.898)
	Treatment P-value [b]		0.00004
	Interaction P-value [c]		0.98609

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Pruritus	No. of Events (%)	74 (36.6)	16 (7.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.578 (3.248, 9.578)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.21843
Rash	No. of Events (%)	35 (17.3)	14 (6.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.600 (1.399, 4.833)
	Treatment P-value [b]		0.00184
	Interaction P-value [c]		0.88476

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 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]		0.00156
	Interaction P-value [c]		0.99329
Rash maculo-papular	No. of Events (%)	39 (19.3)	6 (3.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.073 (2.994, 16.709)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.98782

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Skin hyperpigmentation	No. of Events (%)	13 (6.4)	1 (0.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (26.87, NC)
	Hazard Ratio (95% CI) [a]		12.981 (1.697, 99.287)
	Treatment P-value [b]		0.00146
	Interaction P-value [c]		0.99379

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

3.3 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]		1.017 (0.773, 1.337)
	Treatment P-value [b]		0.79946
	Interaction P-value [c]		0.40204

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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]		0.879 (0.716, 1.078)
	Treatment P-value [b]		0.19077
	Interaction P-value [c]		0.40204

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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]		0.928 (0.773, 1.115)
	Treatment P-value [b]		0.42227
	Interaction P-value [c]		0.92003

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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]		0.92003

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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]		0.993 (0.824, 1.198)
	Treatment P-value [b]		0.98174
	Interaction P-value [c]		0.11949

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)	0.18 (0.13, 0.26)	0.13 (0.10, 0.20)
	Hazard Ratio (95% CI) [a]		0.726 (0.514, 1.026)
	Treatment P-value [b]		0.09242
	Interaction P-value [c]		0.11949

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)	0.21 (0.16, 0.26)	0.13 (0.07, 0.16)
	Hazard Ratio (95% CI) [a]		0.870 (0.674, 1.123)
	Treatment P-value [b]		0.41184
	Interaction P-value [c]		0.73366

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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]		0.877 (0.565, 1.360)
	Treatment P-value [b]		0.39603
	Interaction P-value [c]		0.73366

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (0.779, 1.269)
	Treatment P-value [b]		0.94129
	Interaction P-value [c]		0.73366

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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]		1.035 (0.801, 1.339)
	Treatment P-value [b]		0.75912
	Interaction P-value [c]		0.24620

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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]		0.850 (0.688, 1.051)
	Treatment P-value [b]		0.13286
	Interaction P-value [c]		0.24620

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (0.10, 0.23)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		1.127 (0.834, 1.522)
	Treatment P-value [b]		0.63063
	Interaction P-value [c]		0.11889

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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]		0.847 (0.697, 1.030)
	Treatment P-value [b]		0.10064
	Interaction P-value [c]		0.11889

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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]		1.185 (0.918, 1.530)
	Treatment P-value [b]		0.20495
	Interaction P-value [c]		0.03348

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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]		0.826 (0.620, 1.099)
	Treatment P-value [b]		0.11848
	Interaction P-value [c]		0.03348

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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]		0.706 (0.508, 0.981)
	Treatment P-value [b]		0.05289
	Interaction P-value [c]		0.03348

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)	0.21 (0.13, 0.26)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.870 (0.657, 1.153)
	Treatment P-value [b]		0.28754
	Interaction P-value [c]		0.60237

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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]		0.954 (0.780, 1.167)
	Treatment P-value [b]		0.70481
	Interaction P-value [c]		0.60237

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)	0.16 (0.16, 0.23)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.951 (0.798, 1.133)
	Treatment P-value [b]		0.61731
	Interaction P-value [c]		0.34705

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (0.07, 0.16)
	Hazard Ratio (95% CI) [a]		0.750 (0.472, 1.191)
	Treatment P-value [b]		0.09950
	Interaction P-value [c]		0.34705

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (0.07, 0.20)
	Hazard Ratio (95% CI) [a]		1.054 (0.719, 1.545)
	Treatment P-value [b]		0.85609
	Interaction P-value [c]		0.53562

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)	0.16 (0.16, 0.23)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.920 (0.755, 1.121)
	Treatment P-value [b]		0.36619
	Interaction P-value [c]		0.53562

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

3.4 Subgruppenanalysen zu den nicht schweren (CTCAE Grad < 3) unerwünschten Ereignissen

3.4.1 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]		1.056 (0.803, 1.389)
	Treatment P-value [b]		0.67868
	Interaction P-value [c]		0.57819

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.959 (0.780, 1.177)
	Treatment P-value [b]		0.70510
	Interaction P-value [c]		0.57819

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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=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]		1.003 (0.835, 1.206)
	Treatment P-value [b]		0.94250
	Interaction P-value [c]		0.78340

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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]		0.78340

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: 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]		1.065 (0.883, 1.286)
	Treatment P-value [b]		0.42207
	Interaction P-value [c]		0.12033

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)	0.18 (0.13, 0.26)	0.13 (0.10, 0.20)
	Hazard Ratio (95% CI) [a]		0.779 (0.552, 1.101)
	Treatment P-value [b]		0.22249
	Interaction P-value [c]		0.12033

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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, 0.16)
	Hazard Ratio (95% CI) [a]		0.969 (0.749, 1.254)
	Treatment P-value [b]		0.96897
	Interaction P-value [c]		0.83440

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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]		0.901 (0.581, 1.398)
	Treatment P-value [b]		0.58005
	Interaction P-value [c]		0.83440

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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]		1.040 (0.815, 1.328)
	Treatment P-value [b]		0.70293
	Interaction P-value [c]		0.83440

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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]		1.085 (0.839, 1.402)
	Treatment P-value [b]		0.52747
	Interaction P-value [c]		0.34677

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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]		0.924 (0.746, 1.144)
	Treatment P-value [b]		0.51625
	Interaction P-value [c]		0.34677

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (0.10, 0.23)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		1.093 (0.810, 1.476)
	Treatment P-value [b]		0.71445
	Interaction P-value [c]		0.44353

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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]		0.951 (0.781, 1.157)
	Treatment P-value [b]		0.69342
	Interaction P-value [c]		0.44353

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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]		1.191 (0.922, 1.539)
	Treatment P-value [b]		0.16650
	Interaction P-value [c]		0.16878

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (0.681, 1.207)
	Treatment P-value [b]		0.44570
	Interaction P-value [c]		0.16878

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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]		0.823 (0.591, 1.148)
	Treatment P-value [b]		0.27126
	Interaction P-value [c]		0.16878

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)	0.20 (0.13, 0.26)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.917 (0.691, 1.216)
	Treatment P-value [b]		0.54586
	Interaction P-value [c]		0.50593

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (0.10, 0.20)
	Hazard Ratio (95% CI) [a]		1.031 (0.843, 1.263)
	Treatment P-value [b]		0.65818
	Interaction P-value [c]		0.50593

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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, 0.23)	0.13 (0.13, 0.16)
	Hazard Ratio (95% CI) [a]		1.021 (0.856, 1.218)
	Treatment P-value [b]		0.73485
	Interaction P-value [c]		0.32464

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (0.07, 0.16)
	Hazard Ratio (95% CI) [a]		0.796 (0.501, 1.265)
	Treatment P-value [b]		0.20122
	Interaction P-value [c]		0.32464

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (0.07, 0.20)
	Hazard Ratio (95% CI) [a]		1.036 (0.705, 1.522)
	Treatment P-value [b]		0.92302
	Interaction P-value [c]		0.91700

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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]		1.012 (0.830, 1.235)
	Treatment P-value [b]		0.86503
	Interaction P-value [c]		0.91700

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

3.4.2 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]		1.050 (0.799, 1.381)
	Treatment P-value [b]		0.70181
	Interaction P-value [c]		0.58487

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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=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)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.955 (0.777, 1.173)
	Treatment P-value [b]		0.67919
	Interaction P-value [c]		0.58487

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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=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]		0.997 (0.829, 1.198)
	Treatment P-value [b]		0.99658
	Interaction P-value [c]		0.82686

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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]		0.952 (0.656, 1.381)
	Treatment P-value [b]		0.84224
	Interaction P-value [c]		0.82686

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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]		1.066 (0.883, 1.286)
	Treatment P-value [b]		0.42866
	Interaction P-value [c]		0.09519

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)	0.18 (0.13, 0.26)	0.13 (0.10, 0.20)
	Hazard Ratio (95% CI) [a]		0.762 (0.539, 1.076)
	Treatment P-value [b]		0.17391
	Interaction P-value [c]		0.09519

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: 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]		0.958 (0.741, 1.240)
	Treatment P-value [b]		0.94068
	Interaction P-value [c]		0.82941

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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]		0.904 (0.582, 1.402)
	Treatment P-value [b]		0.58005
	Interaction P-value [c]		0.82941

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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]		1.039 (0.814, 1.326)
	Treatment P-value [b]		0.70899
	Interaction P-value [c]		0.82941

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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]		1.078 (0.833, 1.393)
	Treatment P-value [b]		0.55349
	Interaction P-value [c]		0.35688

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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]		0.921 (0.744, 1.141)
	Treatment P-value [b]		0.49265
	Interaction P-value [c]		0.35688

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (0.10, 0.23)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		1.096 (0.812, 1.479)
	Treatment P-value [b]		0.71445
	Interaction P-value [c]		0.41318

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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]		0.943 (0.775, 1.148)
	Treatment P-value [b]		0.62872
	Interaction P-value [c]		0.41318

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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]		1.174 (0.909, 1.517)
	Treatment P-value [b]		0.20676
	Interaction P-value [c]		0.19881

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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]		0.913 (0.686, 1.216)
	Treatment P-value [b]		0.47732
	Interaction P-value [c]		0.19881

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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]		0.822 (0.590, 1.145)
	Treatment P-value [b]		0.27300
	Interaction P-value [c]		0.19881

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)	0.21 (0.13, 0.26)	0.13 (0.10, 0.16)
	Hazard Ratio (95% CI) [a]		0.916 (0.691, 1.215)
	Treatment P-value [b]		0.54728
	Interaction P-value [c]		0.52699

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: 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 (0.10, 0.20)
	Hazard Ratio (95% CI) [a]		1.025 (0.837, 1.254)
	Treatment P-value [b]		0.72573
	Interaction P-value [c]		0.52699

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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]		1.015 (0.851, 1.211)
	Treatment P-value [b]		0.78366
	Interaction P-value [c]		0.33726

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (0.07, 0.16)
	Hazard Ratio (95% CI) [a]		0.797 (0.502, 1.266)
	Treatment P-value [b]		0.20122
	Interaction P-value [c]		0.33726

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (0.07, 0.20)
	Hazard Ratio (95% CI) [a]		1.032 (0.702, 1.516)
	Treatment P-value [b]		0.92727
	Interaction P-value [c]		0.91648

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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]		1.008 (0.826, 1.229)
	Treatment P-value [b]		0.91961
	Interaction P-value [c]		0.91648

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

3.5 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 (%)	216 (73.0)	200 (68.7)
	Median Survival Est. (95% CI)	1.77 (1.28, 2.27)	1.41 (0.95, 2.14)
	Hazard Ratio (95% CI) [a]		0.964 (0.794, 1.172)
	Treatment P-value [b]		0.73391
	Homogeneity P-value [c]		NA
Blood and lymphatic system disorders	No. of Events (%)	32 (10.8)	71 (24.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.378 (0.248, 0.575)
	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.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)	36 (12.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.470 (0.268, 0.823)
	Treatment P-value [b]		0.00691
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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]		0.12600
	Homogeneity P-value [c]		NA
Gastrointestinal disorders	No. of Events (%)	30 (10.1)	35 (12.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.776 (0.475, 1.269)
	Treatment P-value [b]		0.31248
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	5 (1.7)	6 (2.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.809 (0.247, 2.657)
	Treatment P-value [b]		0.72678
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Diarrhoea	No. of Events (%)	13 (4.4)	5 (1.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.328 (0.821, 6.598)
	Treatment P-value [b]		0.10176
	Homogeneity P-value [c]		NA
General disorders and administration site conditions	No. of Events (%)	43 (14.5)	32 (11.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.251 (0.791, 1.978)
	Treatment P-value [b]		0.33706
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Asthenia	No. of Events (%)	8 (2.7)	8 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.885 (0.331, 2.367)
	Treatment P-value [b]		0.80795
	Homogeneity P-value [c]		NA
Fatigue	No. of Events (%)	21 (7.1)	14 (4.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.425 (0.724, 2.806)
	Treatment P-value [b]		0.30257
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
General physical health deterioration	No. of Events (%)	4 (1.4)	7 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.515 (0.150, 1.766)
	Treatment P-value [b]		0.28249
	Homogeneity P-value [c]		NA
Infections and infestations	No. of Events (%)	58 (19.6)	35 (12.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.624 (1.067, 2.473)
	Treatment P-value [b]		0.02222
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)	7 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.766 (0.703, 4.436)
	Treatment P-value [b]		0.21964
	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]		0.886 (0.309, 2.540)
	Treatment P-value [b]		0.82276
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Urinary tract infection bacterial	No. of Events (%)	13 (4.4)	4 (1.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.066 (0.998, 9.420)
	Treatment P-value [b]		0.03946
	Homogeneity P-value [c]		NA
Investigations	No. of Events (%)	46 (15.5)	64 (22.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.612 (0.418, 0.898)
	Treatment P-value [b]		0.01220
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Lipase increased	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]		1.315 (0.454, 3.806)
	Treatment P-value [b]		0.61236
	Homogeneity P-value [c]		NA
Lymphocyte count decreased	No. of Events (%)	9 (3.0)	13 (4.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.689 (0.294, 1.615)
	Treatment P-value [b]		0.38845
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)	45 (15.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.385 (0.228, 0.649)
	Treatment P-value [b]		0.00022
	Homogeneity P-value [c]		NA
White blood cell count decreased	No. of Events (%)	4 (1.4)	22 (7.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.157 (0.053, 0.462)
	Treatment P-value [b]		0.00013
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)	35 (12.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.906 (1.265, 2.871)
	Treatment P-value [b]		0.00167
	Homogeneity P-value [c]		NA
Decreased appetite	No. of Events (%)	16 (5.4)	8 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.923 (0.822, 4.502)
	Treatment P-value [b]		0.12498
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Dehydration	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]		0.917 (0.265, 3.176)
	Treatment P-value [b]		0.89100
	Homogeneity P-value [c]		NA
Hyperglycaemia	No. of Events (%)	21 (7.1)	3 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.931 (2.066, 23.248)
	Treatment P-value [b]		0.00027
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Hyponatraemia	No. of Events (%)	13 (4.4)	7 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.669 (0.663, 4.200)
	Treatment P-value [b]		0.27064
	Homogeneity P-value [c]		NA
Musculoskeletal and connective tissue disorders	No. of Events (%)	10 (3.4)	16 (5.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.573 (0.260, 1.265)
	Treatment P-value [b]		0.16338
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	No. of Events (%)	20 (6.8)	18 (6.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.055 (0.557, 2.001)
	Treatment P-value [b]		0.86909
	Homogeneity P-value [c]		NA
Malignant neoplasm progression	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]		1.198 (0.516, 2.782)
	Treatment P-value [b]		0.67458
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Nervous system disorders	No. of Events (%)	32 (10.8)	14 (4.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.027 (1.076, 3.818)
	Treatment P-value [b]		0.02560
	Homogeneity P-value [c]		NA
Peripheral sensory neuropathy	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]		1.908 (0.775, 4.698)
	Treatment P-value [b]		0.15270
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Renal and urinary disorders	No. of Events (%)	20 (6.8)	15 (5.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.226 (0.624, 2.407)
	Treatment P-value [b]		0.55389
	Homogeneity P-value [c]		NA
Acute kidney injury	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]		1.844 (0.554, 6.146)
	Treatment P-value [b]		0.31131
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
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
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]		1.491 (0.696, 3.193)
	Treatment P-value [b]		0.30049
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Skin and subcutaneous tissue disorders	No. of Events (%)	51 (17.2)	6 (2.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.370 (3.998, 21.960)
	Treatment P-value [b]		<.00001
	Homogeneity P-value [c]		NA
Drug eruption	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]		4.426 (0.933, 20.989)
	Treatment P-value [b]		0.04095
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Rash maculo-papular	No. of Events (%)	22 (7.4)	1 (0.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		24.770 (3.298, 186.063)
	Treatment P-value [b]		<.00001
	Homogeneity P-value [c]		NA
Vascular disorders	No. of Events (%)	10 (3.4)	10 (3.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.865 (0.356, 2.101)
	Treatment P-value [b]		0.74886
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	71 (67.0)	68 (66.0)
	Median Survival Est. (95% CI)	2.45 (1.81, 4.60)	1.45 (0.82, 2.69)
	Hazard Ratio (95% CI) [a]		0.836 (0.599, 1.166)
	Treatment P-value [b]		0.28671
	Interaction P-value [c]		0.29502
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]		0.693 (0.352, 1.363)
	Treatment P-value [b]		0.30017
	Interaction P-value [c]		0.04206

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
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]		0.822 (0.349, 1.935)
	Treatment P-value [b]		0.67858
	Interaction P-value [c]		0.12301
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

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Infections and infestations	No. of Events (%)	18 (17.0)	11 (10.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.531 (0.723, 3.242)
	Treatment P-value [b]		0.26159
	Interaction P-value [c]		0.85557
Investigations	No. of Events (%)	14 (13.2)	24 (23.3)
	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]		0.03956
	Interaction P-value [c]		0.33568

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
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]		0.284 (0.103, 0.783)
	Treatment P-value [b]		0.01211
	Interaction P-value [c]		0.37661
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]		0.98792

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Metabolism and nutrition disorders	No. of Events (%)	21 (19.8)	8 (7.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.585 (1.145, 5.837)
	Treatment P-value [b]		0.01757
	Interaction P-value [c]		0.42756
Hyperglycaemia	No. of Events (%)	3 (2.8)	2 (1.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.430 (0.239, 8.555)
	Treatment P-value [b]		0.71015
	Interaction P-value [c]		0.06375

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Nervous system disorders	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]		4.337 (0.950, 19.800)
	Treatment P-value [b]		0.04845
	Interaction P-value [c]		0.25936
Skin and subcutaneous tissue disorders	No. of Events (%)	14 (13.2)	1 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		14.007 (1.842, 106.519)
	Treatment P-value [b]		0.00080
	Interaction P-value [c]		0.62015

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
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]		0.99029

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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=190)	Chemotherapy (N=188)
Any Event	No. of Events (%)	145 (76.3)	132 (70.2)
	Median Survival Est. (95% CI)	1.33 (0.92, 1.87)	1.33 (0.72, 2.50)
	Hazard Ratio (95% CI) [a]		1.039 (0.821, 1.316)
	Treatment P-value [b]		0.75559
	Interaction P-value [c]		0.29502
Blood and lymphatic system disorders	No. of Events (%)	17 (8.9)	52 (27.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.281 (0.162, 0.485)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.04206

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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=190)	Chemotherapy (N=188)
Anaemia	No. of Events (%)	9 (4.7)	25 (13.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.333 (0.156, 0.714)
	Treatment P-value [b]		0.00279
	Interaction P-value [c]		0.12301
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.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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=190)	Chemotherapy (N=188)
Infections and infestations	No. of Events (%)	40 (21.1)	24 (12.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.666 (1.004, 2.763)
	Treatment P-value [b]		0.04753
	Interaction P-value [c]		0.85557
Investigations	No. of Events (%)	32 (16.8)	40 (21.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.731 (0.459, 1.164)
	Treatment P-value [b]		0.17720
	Interaction P-value [c]		0.33568

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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=190)	Chemotherapy (N=188)
Neutrophil count decreased	No. of Events (%)	16 (8.4)	30 (16.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.484 (0.264, 0.889)
	Treatment P-value [b]		0.01535
	Interaction P-value [c]		0.37661
White blood cell count decreased	No. of Events (%)	4 (2.1)	15 (8.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.252 (0.084, 0.758)
	Treatment P-value [b]		0.00766
	Interaction P-value [c]		0.98792

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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=190)	Chemotherapy (N=188)
Metabolism and nutrition disorders	No. of Events (%)	46 (24.2)	27 (14.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.765 (1.097, 2.839)
	Treatment P-value [b]		0.01791
	Interaction P-value [c]		0.42756
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]		18.271 (2.439, 136.889)
	Treatment P-value [b]		0.00008
	Interaction P-value [c]		0.06375

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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=190)	Chemotherapy (N=188)
Nervous system disorders	No. of Events (%)	22 (11.6)	12 (6.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.655 (0.819, 3.347)
	Treatment P-value [b]		0.15307
	Interaction P-value [c]		0.25936
Skin and subcutaneous tissue disorders	No. of Events (%)	37 (19.5)	5 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.962 (3.129, 20.265)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.62015

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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=190)	Chemotherapy (N=188)
Rash maculo-papular	No. of Events (%)	14 (7.4)	1 (0.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		14.012 (1.842, 106.591)
	Treatment P-value [b]		0.00085
	Interaction P-value [c]		0.99029

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	174 (71.0)	157 (69.5)
	Median Survival Est. (95% CI)	1.91 (1.45, 2.79)	1.41 (0.76, 2.10)
	Hazard Ratio (95% CI) [a]		0.869 (0.700, 1.078)
	Treatment P-value [b]		0.22609
	Interaction P-value [c]		0.02685
Blood and lymphatic system disorders	No. of Events (%)	30 (12.2)	54 (23.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.452 (0.289, 0.707)
	Treatment P-value [b]		0.00035
	Interaction P-value [c]		0.11088

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)	29 (12.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.526 (0.292, 0.948)
	Treatment P-value [b]		0.02998
	Interaction P-value [c]		0.33139
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.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	46 (18.8)	31 (13.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.318 (0.836, 2.079)
	Treatment P-value [b]		0.23193
	Interaction P-value [c]		0.05951
Investigations	No. of Events (%)	39 (15.9)	52 (23.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.608 (0.401, 0.922)
	Treatment P-value [b]		0.01945
	Interaction P-value [c]		0.70941

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Neutrophil count decreased	No. of Events (%)	20 (8.2)	37 (16.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.443 (0.257, 0.763)
	Treatment P-value [b]		0.00267
	Interaction P-value [c]		0.32873
White blood cell count decreased	No. of Events (%)	3 (1.2)	19 (8.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.136 (0.040, 0.460)
	Treatment P-value [b]		0.00017
	Interaction P-value [c]		0.39086

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Metabolism and nutrition disorders	No. of Events (%)	52 (21.2)	25 (11.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.952 (1.211, 3.145)
	Treatment P-value [b]		0.00517
	Interaction P-value [c]		0.85007
Hyperglycaemia	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]		6.938 (1.586, 30.343)
	Treatment P-value [b]		0.00291
	Interaction P-value [c]		0.92306

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Nervous system disorders	No. of Events (%)	23 (9.4)	8 (3.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.362 (1.056, 5.283)
	Treatment P-value [b]		0.03556
	Interaction P-value [c]		0.72549
Skin and subcutaneous tissue disorders	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]		10.188 (3.653, 28.415)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.62184

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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]		0.99063

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)	43 (66.2)
	Median Survival Est. (95% CI)	0.66 (0.53, 1.77)	2.33 (0.69, 5.78)
	Hazard Ratio (95% CI) [a]		1.490 (0.973, 2.281)
	Treatment P-value [b]		0.08828
	Interaction P-value [c]		0.02685
Blood and lymphatic system disorders	No. of Events (%)	2 (3.9)	17 (26.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.130 (0.030, 0.563)
	Treatment P-value [b]		0.00140
	Interaction P-value [c]		0.11088

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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]		0.179 (0.022, 1.455)
	Treatment P-value [b]		0.06725
	Interaction P-value [c]		0.33139
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.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)	4 (6.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.258 (1.374, 13.200)
	Treatment P-value [b]		0.00592
	Interaction P-value [c]		0.05951
Investigations	No. of Events (%)	7 (13.7)	12 (18.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (25.56, NC)
	Hazard Ratio (95% CI) [a]		0.738 (0.291, 1.876)
	Treatment P-value [b]		0.52639
	Interaction P-value [c]		0.70941

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
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]		0.152 (0.019, 1.214)
	Treatment P-value [b]		0.04276
	Interaction P-value [c]		0.32873
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]		0.419 (0.044, 4.029)
	Treatment P-value [b]		0.44469
	Interaction P-value [c]		0.39086

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
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]		2.135 (0.959, 4.754)
	Treatment P-value [b]		0.05484
	Interaction P-value [c]		0.85007
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]		7.879 (0.948, 65.461)
	Treatment P-value [b]		0.02352
	Interaction P-value [c]		0.92306

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Nervous system disorders	No. of Events (%)	9 (17.6)	6 (9.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.868 (0.665, 5.251)
	Treatment P-value [b]		0.18827
	Interaction P-value [c]		0.72549
Skin and subcutaneous tissue disorders	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]		6.406 (1.384, 29.657)
	Treatment P-value [b]		0.00948
	Interaction P-value [c]		0.62184

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)	1 (1.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.914 (0.808, 59.202)
	Treatment P-value [b]		0.05235
	Interaction P-value [c]		0.99063

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	171 (73.1)	153 (69.9)
	Median Survival Est. (95% CI)	1.81 (1.18, 2.27)	1.31 (0.76, 2.04)
	Hazard Ratio (95% CI) [a]		0.925 (0.744, 1.151)
	Treatment P-value [b]		0.49446
	Interaction P-value [c]		0.52988
Blood and lymphatic system disorders	No. of Events (%)	24 (10.3)	56 (25.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.341 (0.211, 0.550)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.25452

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)	23 (10.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.450 (0.224, 0.906)
	Treatment P-value [b]		0.02346
	Interaction P-value [c]		0.61075
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.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	48 (20.5)	29 (13.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.513 (0.954, 2.400)
	Treatment P-value [b]		0.08123
	Interaction P-value [c]		0.61469
Investigations	No. of Events (%)	32 (13.7)	42 (19.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.644 (0.406, 1.021)
	Treatment P-value [b]		0.06217
	Interaction P-value [c]		0.91536

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Neutrophil count decreased	No. of Events (%)	13 (5.6)	30 (13.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.364 (0.190, 0.697)
	Treatment P-value [b]		0.00168
	Interaction P-value [c]		0.40386
White blood cell count decreased	No. of Events (%)	3 (1.3)	13 (5.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.205 (0.059, 0.721)
	Treatment P-value [b]		0.00620
	Interaction P-value [c]		0.66327

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Metabolism and nutrition disorders	No. of Events (%)	51 (21.8)	28 (12.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.744 (1.100, 2.766)
	Treatment P-value [b]		0.01768
	Interaction P-value [c]		0.33501
Hyperglycaemia	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]		5.916 (1.750, 20.000)
	Treatment P-value [b]		0.00115
	Interaction P-value [c]		0.99138

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Nervous system disorders	No. of Events (%)	28 (12.0)	10 (4.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.279 (1.106, 4.696)
	Treatment P-value [b]		0.02526
	Interaction P-value [c]		0.41656
Skin and subcutaneous tissue disorders	No. of Events (%)	42 (17.9)	2 (0.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		20.771 (5.027, 85.822)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.03489

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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]		0.99026

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Any Event	No. of Events (%)	45 (72.6)	47 (65.3)
	Median Survival Est. (95% CI)	1.74 (0.82, 3.02)	2.17 (0.72, 5.68)
	Hazard Ratio (95% CI) [a]		1.073 (0.713, 1.616)
	Treatment P-value [b]		0.66883
	Interaction P-value [c]		0.52988
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]		0.603 (0.256, 1.423)
	Treatment P-value [b]		0.25074
	Interaction P-value [c]		0.25452

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		0.608 (0.243, 1.524)
	Treatment P-value [b]		0.28340
	Interaction P-value [c]		0.61075
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.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		2.014 (0.732, 5.541)
	Treatment P-value [b]		0.17759
	Interaction P-value [c]		0.61469
Investigations	No. of Events (%)	14 (22.6)	22 (30.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.673 (0.344, 1.316)
	Treatment P-value [b]		0.24780
	Interaction P-value [c]		0.91536

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Neutrophil count decreased	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]		0.575 (0.244, 1.357)
	Treatment P-value [b]		0.22162
	Interaction P-value [c]		0.40386
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]		0.120 (0.015, 0.947)
	Treatment P-value [b]		0.01682
	Interaction P-value [c]		0.66327

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		2.853 (1.174, 6.937)
	Treatment P-value [b]		0.01919
	Interaction P-value [c]		0.33501
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]		0.99138

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Nervous system disorders	No. of Events (%)	4 (6.5)	4 (5.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.192 (0.298, 4.768)
	Treatment P-value [b]		0.84921
	Interaction P-value [c]		0.41656
Skin and subcutaneous tissue disorders	No. of Events (%)	9 (14.5)	4 (5.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.852 (0.878, 9.268)
	Treatment P-value [b]		0.04142
	Interaction P-value [c]		0.03489

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Rash maculo-papular	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]		4.941 (0.552, 44.214)
	Treatment P-value [b]		0.10740
	Interaction P-value [c]		0.99026

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	83 (68.0)	86 (69.9)
	Median Survival Est. (95% CI)	2.79 (1.87, 4.93)	1.45 (0.59, 2.33)
	Hazard Ratio (95% CI) [a]		0.780 (0.577, 1.055)
	Treatment P-value [b]		0.12013
	Interaction P-value [c]		0.05705
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]		0.250 (0.108, 0.581)
	Treatment P-value [b]		0.00065
	Interaction P-value [c]		0.38374

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
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]		0.232 (0.049, 1.093)
	Treatment P-value [b]		0.04779
	Interaction P-value [c]		0.07186
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.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Infections and infestations	No. of Events (%)	23 (18.9)	17 (13.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.303 (0.696, 2.440)
	Treatment P-value [b]		0.41694
	Interaction P-value [c]		0.65731
Investigations	No. of Events (%)	10 (8.2)	18 (14.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (25.56, NC)
	Hazard Ratio (95% CI) [a]		0.518 (0.239, 1.123)
	Treatment P-value [b]		0.08651
	Interaction P-value [c]		0.57610

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
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]		0.136 (0.017, 1.104)
	Treatment P-value [b]		0.02496
	Interaction P-value [c]		0.52999
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]		0.88688

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Metabolism and nutrition disorders	No. of Events (%)	20 (16.4)	14 (11.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.380 (0.697, 2.732)
	Treatment P-value [b]		0.34595
	Interaction P-value [c]		0.44186
Hyperglycaemia	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]		4.947 (1.084, 22.581)
	Treatment P-value [b]		0.02221
	Interaction P-value [c]		0.99100

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Nervous system disorders	No. of Events (%)	18 (14.8)	7 (5.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.390 (0.998, 5.722)
	Treatment P-value [b]		0.04548
	Interaction P-value [c]		0.59243
Skin and subcutaneous tissue disorders	No. of Events (%)	17 (13.9)	2 (1.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		8.677 (2.005, 37.560)
	Treatment P-value [b]		0.00048
	Interaction P-value [c]		0.90943

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Rash maculo-papular	No. of Events (%)	6 (4.9)	1 (0.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.774 (0.695, 47.970)
	Treatment P-value [b]		0.07349
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: 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]		1.626 (0.961, 2.753)
	Treatment P-value [b]		0.08305
	Interaction P-value [c]		0.05705
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]		0.340 (0.107, 1.084)
	Treatment P-value [b]		0.05530
	Interaction P-value [c]		0.38374

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: 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 (0.012, 0.718)
	Treatment P-value [b]		0.00491
	Interaction P-value [c]		0.07186
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.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: 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]		1.697 (0.497, 5.799)
	Treatment P-value [b]		0.41693
	Interaction P-value [c]		0.65731
Investigations	No. of Events (%)	9 (21.4)	8 (20.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.981 (0.378, 2.543)
	Treatment P-value [b]		0.96410
	Interaction P-value [c]		0.57610

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
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]		0.358 (0.093, 1.385)
	Treatment P-value [b]		0.12107
	Interaction P-value [c]		0.52999
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]		0.302 (0.031, 2.902)
	Treatment P-value [b]		0.27179
	Interaction P-value [c]		0.88688

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
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]		2.705 (1.049, 6.973)
	Treatment P-value [b]		0.03944
	Interaction P-value [c]		0.44186
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]		0.99100

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: US

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Nervous system disorders	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]		0.06074
	Interaction P-value [c]		0.59243
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]		0.90943

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: 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]		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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Any Event	No. of Events (%)	100 (75.8)	90 (69.8)
	Median Survival Est. (95% CI)	1.43 (0.95, 2.07)	1.41 (0.53, 2.63)
	Hazard Ratio (95% CI) [a]		0.995 (0.748, 1.324)
	Treatment P-value [b]		0.99289
	Interaction P-value [c]		0.05705
Blood and lymphatic system disorders	No. of Events (%)	21 (15.9)	37 (28.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.498 (0.292, 0.851)
	Treatment P-value [b]		0.00859
	Interaction P-value [c]		0.38374

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Anaemia	No. of Events (%)	16 (12.1)	19 (14.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.793 (0.408, 1.542)
	Treatment P-value [b]		0.48282
	Interaction P-value [c]		0.07186
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.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Infections and infestations	No. of Events (%)	28 (21.2)	14 (10.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.978 (1.041, 3.758)
	Treatment P-value [b]		0.03152
	Interaction P-value [c]		0.65731
Investigations	No. of Events (%)	27 (20.5)	38 (29.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.604 (0.369, 0.990)
	Treatment P-value [b]		0.04875
	Interaction P-value [c]		0.57610

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Neutrophil count decreased	No. of Events (%)	17 (12.9)	31 (24.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.463 (0.256, 0.837)
	Treatment P-value [b]		0.01079
	Interaction P-value [c]		0.52999
White blood cell count decreased	No. of Events (%)	3 (2.3)	17 (13.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.159 (0.046, 0.541)
	Treatment P-value [b]		0.00080
	Interaction P-value [c]		0.88688

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Metabolism and nutrition disorders	No. of Events (%)	32 (24.2)	15 (11.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.235 (1.210, 4.128)
	Treatment P-value [b]		0.00782
	Interaction P-value [c]		0.44186
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]		5.911 (0.711, 49.108)
	Treatment P-value [b]		0.05972
	Interaction P-value [c]		0.99100

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Nervous system disorders	No. of Events (%)	10 (7.6)	7 (5.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.211 (0.460, 3.184)
	Treatment P-value [b]		0.69631
	Interaction P-value [c]		0.59243
Skin and subcutaneous tissue disorders	No. of Events (%)	22 (16.7)	4 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.803 (1.999, 16.842)
	Treatment P-value [b]		0.00029
	Interaction P-value [c]		0.90943

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: 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]		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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Any Event	No. of Events (%)	78 (65.0)	71 (59.7)
	Median Survival Est. (95% CI)	2.43 (1.45, 5.16)	2.17 (0.95, 6.90)
	Hazard Ratio (95% CI) [a]		0.978 (0.709, 1.348)
	Treatment P-value [b]		0.84291
	Interaction P-value [c]		0.89526
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]		0.423 (0.193, 0.929)
	Treatment P-value [b]		0.02809
	Interaction P-value [c]		0.75143

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Anaemia	No. of Events (%)	4 (3.3)	10 (8.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.385 (0.121, 1.229)
	Treatment P-value [b]		0.09538
	Interaction P-value [c]		0.68197
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.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Infections and infestations	No. of Events (%)	18 (15.0)	12 (10.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.455 (0.701, 3.020)
	Treatment P-value [b]		0.30587
	Interaction P-value [c]		0.72834
Investigations	No. of Events (%)	19 (15.8)	37 (31.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.433 (0.249, 0.752)
	Treatment P-value [b]		0.00271
	Interaction P-value [c]		0.05313

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Neutrophil count decreased	No. of Events (%)	9 (7.5)	30 (25.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.257 (0.122, 0.540)
	Treatment P-value [b]		0.00014
	Interaction P-value [c]		0.05365
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]		0.198 (0.057, 0.690)
	Treatment P-value [b]		0.00498
	Interaction P-value [c]		0.66886

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Metabolism and nutrition disorders	No. of Events (%)	25 (20.8)	10 (8.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.679 (1.286, 5.578)
	Treatment P-value [b]		0.00733
	Interaction P-value [c]		0.27842
Hyperglycaemia	No. of Events (%)	8 (6.7)	1 (0.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		8.186 (1.024, 65.449)
	Treatment P-value [b]		0.01851
	Interaction P-value [c]		0.84067

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: 0

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=120)	Chemotherapy (N=119)
Nervous system disorders	No. of Events (%)	12 (10.0)	6 (5.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.909 (0.716, 5.087)
	Treatment P-value [b]		0.18837
	Interaction P-value [c]		0.89273
Skin and subcutaneous tissue disorders	No. of Events (%)	27 (22.5)	3 (2.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		10.293 (3.122, 33.938)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.75610

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: 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]		0.98896

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Any Event	No. of Events (%)	138 (78.4)	129 (75.0)
	Median Survival Est. (95% CI)	1.38 (0.95, 1.87)	1.26 (0.66, 1.71)
	Hazard Ratio (95% CI) [a]		0.952 (0.748, 1.210)
	Treatment P-value [b]		0.76843
	Interaction P-value [c]		0.89526
Blood and lymphatic system disorders	No. of Events (%)	23 (13.1)	51 (29.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.364 (0.222, 0.596)
	Treatment P-value [b]		0.00003
	Interaction P-value [c]		0.75143

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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]		0.508 (0.269, 0.960)
	Treatment P-value [b]		0.03308
	Interaction P-value [c]		0.68197
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.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	40 (22.7)	23 (13.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.704 (1.020, 2.846)
	Treatment P-value [b]		0.04062
	Interaction P-value [c]		0.72834
Investigations	No. of Events (%)	27 (15.3)	27 (15.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.923 (0.541, 1.575)
	Treatment P-value [b]		0.76469
	Interaction P-value [c]		0.05313

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Neutrophil count decreased	No. of Events (%)	12 (6.8)	15 (8.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.731 (0.342, 1.562)
	Treatment P-value [b]		0.38145
	Interaction P-value [c]		0.05365
White blood cell count decreased	No. of Events (%)	1 (0.6)	8 (4.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.117 (0.015, 0.934)
	Treatment P-value [b]		0.01389
	Interaction P-value [c]		0.66886

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Metabolism and nutrition disorders	No. of Events (%)	42 (23.9)	25 (14.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.642 (1.001, 2.694)
	Treatment P-value [b]		0.04851
	Interaction P-value [c]		0.27842
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]		6.297 (1.421, 27.915)
	Treatment P-value [b]		0.00507
	Interaction P-value [c]		0.84067

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Nervous system disorders	No. of Events (%)	20 (11.4)	8 (4.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.084 (0.917, 4.736)
	Treatment P-value [b]		0.07302
	Interaction P-value [c]		0.89273
Skin and subcutaneous tissue disorders	No. of Events (%)	24 (13.6)	3 (1.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.872 (2.370, 26.147)
	Treatment P-value [b]		0.00007
	Interaction P-value [c]		0.75610

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Rash maculo-papular	No. of Events (%)	12 (6.8)	1 (0.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		11.365 (1.477, 87.431)
	Treatment P-value [b]		0.00343
	Interaction P-value [c]		0.98896

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)	58 (66.7)
	Median Survival Est. (95% CI)	0.95 (0.62, 2.14)	1.68 (0.72, 2.79)
	Hazard Ratio (95% CI) [a]		1.168 (0.824, 1.654)
	Treatment P-value [b]		0.38768
	Interaction P-value [c]		0.18934
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 (0.240, 1.168)
	Treatment P-value [b]		0.12252
	Interaction P-value [c]		0.38055

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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]		1.093 (0.333, 3.581)
	Treatment P-value [b]		0.85672
	Interaction P-value [c]		0.13193
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.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	22 (23.9)	15 (17.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.387 (0.719, 2.674)
	Treatment P-value [b]		0.32156
	Interaction P-value [c]		0.56986
Investigations	No. of Events (%)	16 (17.4)	12 (13.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.217 (0.576, 2.573)
	Treatment P-value [b]		0.61798
	Interaction P-value [c]		0.04932

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Neutrophil count decreased	No. of Events (%)	8 (8.7)	8 (9.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.898 (0.337, 2.393)
	Treatment P-value [b]		0.79237
	Interaction P-value [c]		0.07453
White blood cell count decreased	No. of Events (%)	0	4 (4.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.02979
	Interaction P-value [c]		0.98964

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
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]		2.331 (1.109, 4.900)
	Treatment P-value [b]		0.01870
	Interaction P-value [c]		0.56278
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]		0.98988

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.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Nervous system disorders	No. of Events (%)	8 (8.7)	4 (4.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.556 (0.468, 5.175)
	Treatment P-value [b]		0.46505
	Interaction P-value [c]		0.61392
Skin and subcutaneous tissue disorders	No. of Events (%)	17 (18.5)	2 (2.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		8.548 (1.974, 37.007)
	Treatment P-value [b]		0.00061
	Interaction P-value [c]		0.95010

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)	1 (1.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.665 (1.237, 75.532)
	Treatment P-value [b]		0.00898
	Interaction P-value [c]		0.98807

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	146 (71.6)	142 (69.6)
	Median Survival Est. (95% CI)	1.87 (1.45, 2.79)	1.38 (0.69, 2.27)
	Hazard Ratio (95% CI) [a]		0.883 (0.700, 1.112)
	Treatment P-value [b]		0.32691
	Interaction P-value [c]		0.18934
Blood and lymphatic system disorders	No. of Events (%)	22 (10.8)	55 (27.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.349 (0.213, 0.573)
	Treatment P-value [b]		0.00001
	Interaction P-value [c]		0.38055

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)	31 (15.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.387 (0.202, 0.739)
	Treatment P-value [b]		0.00272
	Interaction P-value [c]		0.13193
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.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	36 (17.6)	20 (9.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.777 (1.029, 3.069)
	Treatment P-value [b]		0.03613
	Interaction P-value [c]		0.56986
Investigations	No. of Events (%)	30 (14.7)	52 (25.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.507 (0.323, 0.795)
	Treatment P-value [b]		0.00277
	Interaction P-value [c]		0.04932

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Neutrophil count decreased	No. of Events (%)	13 (6.4)	37 (18.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.311 (0.165, 0.585)
	Treatment P-value [b]		0.00014
	Interaction P-value [c]		0.07453
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]		0.208 (0.070, 0.614)
	Treatment P-value [b]		0.00181
	Interaction P-value [c]		0.98964

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Metabolism and nutrition disorders	No. of Events (%)	44 (21.6)	25 (12.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.792 (1.097, 2.929)
	Treatment P-value [b]		0.01760
	Interaction P-value [c]		0.56278
Hyperglycaemia	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]		5.009 (1.450, 17.302)
	Treatment P-value [b]		0.00464
	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.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Nervous system disorders	No. of Events (%)	24 (11.8)	10 (4.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.237 (1.069, 4.678)
	Treatment P-value [b]		0.02699
	Interaction P-value [c]		0.61392
Skin and subcutaneous tissue disorders	No. of Events (%)	34 (16.7)	4 (2.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.052 (3.212, 25.510)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.95010

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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]		0.98807

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	104 (74.3)	62 (57.9)
	Median Survival Est. (95% CI)	1.71 (1.12, 2.73)	4.96 (2.69, 12.78)
	Hazard Ratio (95% CI) [a]		1.482 (1.081, 2.030)
	Treatment P-value [b]		0.00745
	Interaction P-value [c]		0.00154
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]		0.730 (0.380, 1.402)
	Treatment P-value [b]		0.31768
	Interaction P-value [c]		0.06861

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		1.228 (0.537, 2.807)
	Treatment P-value [b]		0.62880
	Interaction P-value [c]		0.01216
Infections and infestations	No. of Events (%)	32 (22.9)	10 (9.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.494 (1.226, 5.074)
	Treatment P-value [b]		0.00843
	Interaction P-value [c]		0.20253

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Investigations	No. of Events (%)	26 (18.6)	17 (15.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (25.56, NC)
	Hazard Ratio (95% CI) [a]		1.140 (0.618, 2.101)
	Treatment P-value [b]		0.68094
	Interaction P-value [c]		0.05555
Neutrophil count decreased	No. of Events (%)	14 (10.0)	11 (10.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.938 (0.426, 2.067)
	Treatment P-value [b]		0.85011
	Interaction P-value [c]		0.03436

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		0.752 (0.047, 12.030)
	Treatment P-value [b]		0.83621
	Interaction P-value [c]		0.65167
Metabolism and nutrition disorders	No. of Events (%)	33 (23.6)	4 (3.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.983 (2.474, 19.710)
	Treatment P-value [b]		0.00002
	Interaction P-value [c]		0.00783

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		7.702 (0.986, 60.170)
	Treatment P-value [b]		0.02104
	Interaction P-value [c]		0.80167
Nervous system disorders	No. of Events (%)	17 (12.1)	12 (11.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.951 (0.454, 1.991)
	Treatment P-value [b]		0.85533
	Interaction P-value [c]		0.38898

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Skin and subcutaneous tissue disorders	No. of Events (%)	28 (20.0)	3 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.650 (2.325, 25.167)
	Treatment P-value [b]		0.00008
	Interaction P-value [c]		0.39591
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]		0.99992

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Any Event	No. of Events (%)	61 (71.8)	80 (73.4)
	Median Survival Est. (95% CI)	1.18 (0.72, 1.91)	0.72 (0.26, 1.45)
	Hazard Ratio (95% CI) [a]		0.806 (0.577, 1.125)
	Treatment P-value [b]		0.20177
	Interaction P-value [c]		0.00154
Blood and lymphatic system disorders	No. of Events (%)	9 (10.6)	33 (30.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.296 (0.142, 0.619)
	Treatment P-value [b]		0.00064
	Interaction P-value [c]		0.06861

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: 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, 0.455)
	Treatment P-value [b]		0.00026
	Interaction P-value [c]		0.01216
Infections and infestations	No. of Events (%)	14 (16.5)	17 (15.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.000 (0.493, 2.029)
	Treatment P-value [b]		0.99946
	Interaction P-value [c]		0.20253

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Investigations	No. of Events (%)	16 (18.8)	35 (32.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.466 (0.258, 0.842)
	Treatment P-value [b]		0.01663
	Interaction P-value [c]		0.05555
Neutrophil count decreased	No. of Events (%)	6 (7.1)	29 (26.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.210 (0.087, 0.505)
	Treatment P-value [b]		0.00022
	Interaction P-value [c]		0.03436

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
White blood cell count decreased	No. of Events (%)	3 (3.5)	19 (17.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.180 (0.053, 0.609)
	Treatment P-value [b]		0.00202
	Interaction P-value [c]		0.65167
Metabolism and nutrition disorders	No. of Events (%)	21 (24.7)	17 (15.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.629 (0.859, 3.089)
	Treatment P-value [b]		0.13617
	Interaction P-value [c]		0.00783

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
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]		0.80167
Nervous system disorders	No. of Events (%)	6 (7.1)	2 (1.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.272 (0.660, 16.220)
	Treatment P-value [b]		0.10887
	Interaction P-value [c]		0.38898

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: 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)	1 (0.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		22.304 (2.958, 168.204)
	Treatment P-value [b]		0.00001
	Interaction P-value [c]		0.39591
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]		0.99992

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: Vinflunine

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Any Event	No. of Events (%)	51 (71.8)	58 (77.3)
	Median Survival Est. (95% CI)	2.10 (1.25, 4.93)	0.46 (0.30, 1.25)
	Hazard Ratio (95% CI) [a]		0.636 (0.436, 0.926)
	Treatment P-value [b]		0.01948
	Interaction P-value [c]		0.00154
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]		0.217 (0.081, 0.577)
	Treatment P-value [b]		0.00104
	Interaction P-value [c]		0.06861

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: Vinflunine

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Anaemia	No. of Events (%)	2 (2.8)	6 (8.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.341 (0.069, 1.690)
	Treatment P-value [b]		0.16334
	Interaction P-value [c]		0.01216
Infections and infestations	No. of Events (%)	12 (16.9)	8 (10.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.597 (0.653, 3.907)
	Treatment P-value [b]		0.32434
	Interaction P-value [c]		0.20253

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: Vinflunine

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Investigations	No. of Events (%)	4 (5.6)	12 (16.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.335 (0.108, 1.038)
	Treatment P-value [b]		0.04186
	Interaction P-value [c]		0.05555
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]		0.205 (0.024, 1.757)
	Treatment P-value [b]		0.10872
	Interaction P-value [c]		0.03436

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: Vinflunine

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
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]		0.65167
Metabolism and nutrition disorders	No. of Events (%)	13 (18.3)	14 (18.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.916 (0.431, 1.950)
	Treatment P-value [b]		0.83248
	Interaction P-value [c]		0.00783

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: Vinflunine

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Hyperglycaemia	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]		3.183 (0.642, 15.774)
	Treatment P-value [b]		0.13496
	Interaction P-value [c]		0.80167
Nervous system disorders	No. of Events (%)	9 (12.7)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.00219
	Interaction P-value [c]		0.38898

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: 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)	2 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.773 (0.784, 18.163)
	Treatment P-value [b]		0.07292
	Interaction P-value [c]		0.39591
Rash maculo-papular	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]		3.106 (0.323, 29.860)
	Treatment P-value [b]		0.32651
	Interaction P-value [c]		0.99992

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Any Event	No. of Events (%)	75 (78.1)	69 (67.6)
	Median Survival Est. (95% CI)	1.25 (0.72, 2.33)	1.71 (0.66, 2.79)
	Hazard Ratio (95% CI) [a]		1.112 (0.802, 1.543)
	Treatment P-value [b]		0.52240
	Interaction P-value [c]		0.28461
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]		0.705 (0.370, 1.343)
	Treatment P-value [b]		0.29388
	Interaction P-value [c]		0.02601

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: 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]		1.146 (0.487, 2.700)
	Treatment P-value [b]		0.73900
	Interaction P-value [c]		0.01379
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.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Infections and infestations	No. of Events (%)	15 (15.6)	11 (10.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.438 (0.660, 3.130)
	Treatment P-value [b]		0.35835
	Interaction P-value [c]		0.74329
Investigations	No. of Events (%)	17 (17.7)	26 (25.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.620 (0.336, 1.143)
	Treatment P-value [b]		0.12781
	Interaction P-value [c]		0.88647

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
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]		0.506 (0.235, 1.087)
	Treatment P-value [b]		0.08410
	Interaction P-value [c]		0.52664
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]		0.110 (0.014, 0.869)
	Treatment P-value [b]		0.01194
	Interaction P-value [c]		0.60666

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Metabolism and nutrition disorders	No. of Events (%)	24 (25.0)	13 (12.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.044 (1.040, 4.014)
	Treatment P-value [b]		0.03630
	Interaction P-value [c]		0.87276
Hyperglycaemia	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]		3.176 (0.641, 15.738)
	Treatment P-value [b]		0.14540
	Interaction P-value [c]		0.25127

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Nervous system disorders	No. of Events (%)	12 (12.5)	6 (5.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.008 (0.754, 5.352)
	Treatment P-value [b]		0.14998
	Interaction P-value [c]		0.95296
Skin and subcutaneous tissue disorders	No. of Events (%)	21 (21.9)	4 (3.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.214 (2.132, 18.108)
	Treatment P-value [b]		0.00015
	Interaction P-value [c]		0.34163

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: 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]		0.99069

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Any Event	No. of Events (%)	141 (70.5)	131 (69.3)
	Median Survival Est. (95% CI)	1.87 (1.41, 2.79)	1.41 (0.76, 2.37)
	Hazard Ratio (95% CI) [a]		0.892 (0.703, 1.132)
	Treatment P-value [b]		0.35933
	Interaction P-value [c]		0.28461
Blood and lymphatic system disorders	No. of Events (%)	16 (8.0)	49 (25.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.267 (0.152, 0.469)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.02601

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Anaemia	No. of Events (%)	8 (4.0)	26 (13.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.265 (0.120, 0.585)
	Treatment P-value [b]		0.00034
	Interaction P-value [c]		0.01379
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.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Infections and infestations	No. of Events (%)	43 (21.5)	24 (12.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.678 (1.018, 2.765)
	Treatment P-value [b]		0.04089
	Interaction P-value [c]		0.74329
Investigations	No. of Events (%)	29 (14.5)	38 (20.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.656 (0.405, 1.064)
	Treatment P-value [b]		0.08451
	Interaction P-value [c]		0.88647

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Neutrophil count decreased	No. of Events (%)	11 (5.5)	26 (13.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.361 (0.178, 0.731)
	Treatment P-value [b]		0.00298
	Interaction P-value [c]		0.52664
White blood cell count decreased	No. of Events (%)	3 (1.5)	13 (6.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.208 (0.059, 0.729)
	Treatment P-value [b]		0.00658
	Interaction P-value [c]		0.60666

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Metabolism and nutrition disorders	No. of Events (%)	43 (21.5)	22 (11.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.907 (1.141, 3.188)
	Treatment P-value [b]		0.01181
	Interaction P-value [c]		0.87276
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]		14.380 (1.900, 108.810)
	Treatment P-value [b]		0.00056
	Interaction P-value [c]		0.25127

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Nervous system disorders	No. of Events (%)	20 (10.0)	8 (4.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.087 (0.919, 4.741)
	Treatment P-value [b]		0.07623
	Interaction P-value [c]		0.95296
Skin and subcutaneous tissue disorders	No. of Events (%)	30 (15.0)	2 (1.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		14.784 (3.535, 61.833)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.34163

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Rash maculo-papular	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]		11.255 (1.463, 86.571)
	Treatment P-value [b]		0.00364
	Interaction P-value [c]		0.99069

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	189 (73.0)	175 (68.6)
	Median Survival Est. (95% CI)	1.64 (1.18, 2.10)	1.64 (0.95, 2.27)
	Hazard Ratio (95% CI) [a]		0.986 (0.803, 1.212)
	Treatment P-value [b]		0.90288
	Interaction P-value [c]		0.46288
Blood and lymphatic system disorders	No. of Events (%)	28 (10.8)	61 (23.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.398 (0.254, 0.622)
	Treatment P-value [b]		0.00003
	Interaction P-value [c]		0.81857

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Anaemia	No. of Events (%)	17 (6.6)	29 (11.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.543 (0.298, 0.988)
	Treatment P-value [b]		0.04295
	Interaction P-value [c]		0.35505
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.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Infections and infestations	No. of Events (%)	51 (19.7)	30 (11.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.663 (1.059, 2.611)
	Treatment P-value [b]		0.02591
	Interaction P-value [c]		0.73229
Investigations	No. of Events (%)	35 (13.5)	58 (22.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.530 (0.348, 0.806)
	Treatment P-value [b]		0.00270
	Interaction P-value [c]		0.02920

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Neutrophil count decreased	No. of Events (%)	15 (5.8)	40 (15.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.331 (0.183, 0.600)
	Treatment P-value [b]		0.00013
	Interaction P-value [c]		0.07580
White blood cell count decreased	No. of Events (%)	2 (0.8)	20 (7.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.093 (0.022, 0.397)
	Treatment P-value [b]		0.00006
	Interaction P-value [c]		0.06227

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Metabolism and nutrition disorders	No. of Events (%)	61 (23.6)	30 (11.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.090 (1.350, 3.236)
	Treatment P-value [b]		0.00075
	Interaction P-value [c]		0.34361
Hyperglycaemia	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]		6.618 (1.966, 22.277)
	Treatment P-value [b]		0.00042
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Nervous system disorders	No. of Events (%)	28 (10.8)	12 (4.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.072 (1.053, 4.077)
	Treatment P-value [b]		0.03297
	Interaction P-value [c]		0.87978
Skin and subcutaneous tissue disorders	No. of Events (%)	47 (18.1)	5 (2.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.971 (3.965, 25.074)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.43276

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Rash maculo-papular	No. of Events (%)	22 (8.5)	1 (0.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		21.905 (2.952, 162.524)
	Treatment P-value [b]		0.00001
	Interaction P-value [c]		0.99911

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Any Event	No. of Events (%)	27 (73.0)	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]		0.793 (0.460, 1.367)
	Treatment P-value [b]		0.43225
	Interaction P-value [c]		0.46288
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]		0.344 (0.108, 1.096)
	Treatment P-value [b]		0.06008
	Interaction P-value [c]		0.81857

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Anaemia	No. of Events (%)	2 (5.4)	7 (19.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.246 (0.051, 1.182)
	Treatment P-value [b]		0.06060
	Interaction P-value [c]		0.35505
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.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Infections and infestations	No. of Events (%)	7 (18.9)	5 (13.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.341 (0.426, 4.226)
	Treatment P-value [b]		0.61683
	Interaction P-value [c]		0.73229
Investigations	No. of Events (%)	11 (29.7)	6 (16.7)
	Median Survival Est. (95% CI)	NC (6.83, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.763 (0.652, 4.769)
	Treatment P-value [b]		0.27568
	Interaction P-value [c]		0.02920

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		1.102 (0.336, 3.612)
	Treatment P-value [b]		0.88123
	Interaction P-value [c]		0.07580
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]		0.945 (0.133, 6.707)
	Treatment P-value [b]		0.97162
	Interaction P-value [c]		0.06227

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		1.134 (0.346, 3.717)
	Treatment P-value [b]		0.79568
	Interaction P-value [c]		0.34361
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]		0.99086

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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Nervous system disorders	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]		1.800 (0.329, 9.831)
	Treatment P-value [b]		0.45021
	Interaction P-value [c]		0.87978
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]		3.850 (0.430, 34.453)
	Treatment P-value [b]		0.18885
	Interaction P-value [c]		0.43276

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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]		0.99911

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	48 (78.7)	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]		1.115 (0.713, 1.745)
	Treatment P-value [b]		0.55626
	Interaction P-value [c]		0.48749
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]		0.289 (0.102, 0.821)
	Treatment P-value [b]		0.01416
	Interaction P-value [c]		0.45490

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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]		0.121 (0.015, 1.005)
	Treatment P-value [b]		0.02218
	Interaction P-value [c]		0.15562
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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	12 (19.7)	6 (12.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.551 (0.582, 4.133)
	Treatment P-value [b]		0.41019
	Interaction P-value [c]		0.81150
Investigations	No. of Events (%)	13 (21.3)	11 (22.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.890 (0.399, 1.986)
	Treatment P-value [b]		0.80798
	Interaction P-value [c]		0.25429

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		0.537 (0.170, 1.691)
	Treatment P-value [b]		0.27761
	Interaction P-value [c]		0.53259
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]		0.384 (0.035, 4.240)
	Treatment P-value [b]		0.42610
	Interaction P-value [c]		0.38699

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		2.451 (0.966, 6.216)
	Treatment P-value [b]		0.04919
	Interaction P-value [c]		0.40074
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]		0.99191

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Nervous system disorders	No. of Events (%)	9 (14.8)	2 (4.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.222 (0.696, 14.919)
	Treatment P-value [b]		0.12014
	Interaction P-value [c]		0.44713
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]		0.98760

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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]		0.99174

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Any Event	No. of Events (%)	145 (71.8)	139 (68.8)
	Median Survival Est. (95% CI)	1.71 (1.18, 2.37)	1.31 (0.59, 2.27)
	Hazard Ratio (95% CI) [a]		0.933 (0.739, 1.177)
	Treatment P-value [b]		0.56140
	Interaction P-value [c]		0.48749
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]		0.45490

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Anaemia	No. of Events (%)	14 (6.9)	22 (10.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.604 (0.309, 1.181)
	Treatment P-value [b]		0.13410
	Interaction P-value [c]		0.15562
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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Infections and infestations	No. of Events (%)	42 (20.8)	24 (11.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.773 (1.074, 2.928)
	Treatment P-value [b]		0.02237
	Interaction P-value [c]		0.81150
Investigations	No. of Events (%)	26 (12.9)	45 (22.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.516 (0.318, 0.836)
	Treatment P-value [b]		0.00636
	Interaction P-value [c]		0.25429

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Neutrophil count decreased	No. of Events (%)	12 (5.9)	31 (15.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.352 (0.181, 0.685)
	Treatment P-value [b]		0.00141
	Interaction P-value [c]		0.53259
White blood cell count decreased	No. of Events (%)	2 (1.0)	17 (8.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.111 (0.026, 0.481)
	Treatment P-value [b]		0.00037
	Interaction P-value [c]		0.38699

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Metabolism and nutrition disorders	No. of Events (%)	40 (19.8)	26 (12.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.560 (0.952, 2.556)
	Treatment P-value [b]		0.07790
	Interaction P-value [c]		0.40074
Hyperglycaemia	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]		4.362 (1.243, 15.309)
	Treatment P-value [b]		0.01251
	Interaction P-value [c]		0.99191

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Nervous system disorders	No. of Events (%)	18 (8.9)	10 (5.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.656 (0.764, 3.588)
	Treatment P-value [b]		0.19403
	Interaction P-value [c]		0.44713
Skin and subcutaneous tissue disorders	No. of Events (%)	34 (16.8)	6 (3.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.023 (2.528, 14.349)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.98760

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Rash maculo-papular	No. of Events (%)	19 (9.4)	1 (0.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		19.422 (2.600, 145.101)
	Treatment P-value [b]		0.00005
	Interaction P-value [c]		0.99174

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

3.6 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 (%)	70 (66.0)	65 (63.1)
	Median Survival Est. (95% CI)	2.53 (1.81, 5.13)	1.61 (0.95, 4.76)
	Hazard Ratio (95% CI) [a]		0.877 (0.625, 1.229)
	Treatment P-value [b]		0.43762
	Interaction P-value [c]		0.42350

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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=190)	Chemotherapy (N=188)
Any Event	No. of Events (%)	141 (74.2)	130 (69.1)
	Median Survival Est. (95% CI)	1.35 (0.92, 1.87)	1.69 (0.79, 2.53)
	Hazard Ratio (95% CI) [a]		1.038 (0.818, 1.318)
	Treatment P-value [b]		0.76819
	Interaction P-value [c]		0.42350

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	169 (69.0)	153 (67.7)
	Median Survival Est. (95% CI)	1.94 (1.45, 2.83)	1.45 (0.99, 2.20)
	Hazard Ratio (95% CI) [a]		0.882 (0.709, 1.098)
	Treatment P-value [b]		0.28689
	Interaction P-value [c]		0.02697

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)	42 (64.6)
	Median Survival Est. (95% CI)	0.69 (0.53, 1.77)	2.33 (0.69, 17.97)
	Hazard Ratio (95% CI) [a]		1.518 (0.989, 2.331)
	Treatment P-value [b]		0.07655
	Interaction P-value [c]		0.02697

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	166 (70.9)	149 (68.0)
	Median Survival Est. (95% CI)	1.81 (1.28, 2.37)	1.41 (0.85, 2.20)
	Hazard Ratio (95% CI) [a]		0.933 (0.748, 1.165)
	Treatment P-value [b]		0.54933
	Interaction P-value [c]		0.45450

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)	46 (63.9)
	Median Survival Est. (95% CI)	1.74 (0.82, 3.02)	2.63 (0.82, 5.78)
	Hazard Ratio (95% CI) [a]		1.116 (0.739, 1.683)
	Treatment P-value [b]		0.53185
	Interaction P-value [c]		0.45450

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	80 (65.6)	83 (67.5)
	Median Survival Est. (95% CI)	2.83 (1.91, 5.06)	1.64 (0.79, 2.79)
	Hazard Ratio (95% CI) [a]		0.796 (0.585, 1.082)
	Treatment P-value [b]		0.15912
	Interaction P-value [c]		0.09144

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: 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]		1.558 (0.917, 2.647)
	Treatment P-value [b]		0.11712
	Interaction P-value [c]		0.09144

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	99 (75.0)	88 (68.2)
	Median Survival Est. (95% CI)	1.43 (0.95, 2.14)	1.41 (0.59, 2.79)
	Hazard Ratio (95% CI) [a]		1.021 (0.766, 1.361)
	Treatment P-value [b]		0.85331
	Interaction P-value [c]		0.09144

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	77 (64.2)	70 (58.8)
	Median Survival Est. (95% CI)	2.53 (1.45, 5.55)	2.27 (0.99, 11.99)
	Hazard Ratio (95% CI) [a]		0.992 (0.718, 1.372)
	Treatment P-value [b]		0.91046
	Interaction P-value [c]		0.89602

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	134 (76.1)	125 (72.7)
	Median Survival Est. (95% CI)	1.41 (1.02, 1.94)	1.35 (0.82, 2.10)
	Hazard Ratio (95% CI) [a]		0.966 (0.757, 1.233)
	Treatment P-value [b]		0.86490
	Interaction P-value [c]		0.89602

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)	56 (64.4)
	Median Survival Est. (95% CI)	0.95 (0.66, 2.33)	1.94 (0.85, 4.44)
	Hazard Ratio (95% CI) [a]		1.137 (0.796, 1.624)
	Treatment P-value [b]		0.48451
	Interaction P-value [c]		0.31282

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	145 (71.1)	139 (68.1)
	Median Survival Est. (95% CI)	1.87 (1.45, 2.79)	1.41 (0.82, 2.37)
	Hazard Ratio (95% CI) [a]		0.914 (0.724, 1.153)
	Treatment P-value [b]		0.49314
	Interaction P-value [c]		0.31282

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	103 (73.6)	60 (56.1)
	Median Survival Est. (95% CI)	1.71 (1.12, 2.73)	5.52 (2.79, 25.56)
	Hazard Ratio (95% CI) [a]		1.515 (1.101, 2.083)
	Treatment P-value [b]		0.00536
	Interaction P-value [c]		0.00160

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)	78 (71.6)
	Median Survival Est. (95% CI)	1.18 (0.72, 2.27)	0.82 (0.30, 1.68)
	Hazard Ratio (95% CI) [a]		0.812 (0.579, 1.138)
	Treatment P-value [b]		0.22290
	Interaction P-value [c]		0.00160

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Vinflunine

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Any Event	No. of Events (%)	49 (69.0)	57 (76.0)
	Median Survival Est. (95% CI)	2.10 (1.28, 4.93)	0.69 (0.36, 1.64)
	Hazard Ratio (95% CI) [a]		0.647 (0.442, 0.948)
	Treatment P-value [b]		0.02639
	Interaction P-value [c]		0.00160

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Any Event	No. of Events (%)	74 (77.1)	68 (66.7)
	Median Survival Est. (95% CI)	1.25 (0.76, 2.33)	1.74 (0.82, 2.79)
	Hazard Ratio (95% CI) [a]		1.119 (0.805, 1.556)
	Treatment P-value [b]		0.49775
	Interaction P-value [c]		0.32015

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	137 (68.5)	127 (67.2)
	Median Survival Est. (95% CI)	1.91 (1.41, 2.83)	1.45 (0.82, 2.69)
	Hazard Ratio (95% CI) [a]		0.910 (0.715, 1.159)
	Treatment P-value [b]		0.45832
	Interaction P-value [c]		0.32015

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Any Event	No. of Events (%)	186 (71.8)	172 (67.5)
	Median Survival Est. (95% CI)	1.64 (1.18, 2.14)	1.68 (1.18, 2.53)
	Hazard Ratio (95% CI) [a]		0.998 (0.811, 1.228)
	Treatment P-value [b]		0.99177
	Interaction P-value [c]		0.54830

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	25 (67.6)	23 (63.9)
	Median Survival Est. (95% CI)	3.55 (1.18, 5.85)	1.18 (0.26, NC)
	Hazard Ratio (95% CI) [a]		0.830 (0.471, 1.462)
	Treatment P-value [b]		0.54742
	Interaction P-value [c]		0.54830

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	47 (77.0)	30 (61.2)
	Median Survival Est. (95% CI)	1.71 (0.82, 2.79)	2.04 (0.30, NC)
	Hazard Ratio (95% CI) [a]		1.208 (0.764, 1.911)
	Treatment P-value [b]		0.38251
	Interaction P-value [c]		0.31643

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	141 (69.8)	137 (67.8)
	Median Survival Est. (95% CI)	1.77 (1.18, 2.73)	1.41 (0.79, 2.33)
	Hazard Ratio (95% CI) [a]		0.928 (0.734, 1.175)
	Treatment P-value [b]		0.54125
	Interaction P-value [c]		0.31643

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

3.7 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 (%)	143 (48.3)	135 (46.4)
	Median Survival Est. (95% CI)	14.36 (5.45, NC)	NC (5.26, NC)
	Hazard Ratio (95% CI) [a]		0.944 (0.745, 1.196)
	Treatment P-value [b]		0.64328
	Homogeneity P-value [c]		0.02188
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.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	9 (3.0)	9 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.989 (0.391, 2.497)
	Treatment P-value [b]		0.98064
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	23 (7.8)	27 (9.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.804 (0.460, 1.403)
	Treatment P-value [b]		0.44189
	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.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Diarrhoea	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]		1.923 (0.578, 6.395)
	Treatment P-value [b]		0.27795
	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, 1.593)
	Treatment P-value [b]		0.74198
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	57 (19.3)	38 (13.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.445 (0.957, 2.180)
	Treatment P-value [b]		0.07719
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Pneumonia	No. of Events (%)	12 (4.1)	9 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.255 (0.528, 2.985)
	Treatment P-value [b]		0.60651
	Homogeneity P-value [c]		NA
Urinary tract infection	No. of Events (%)	8 (2.7)	7 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.038 (0.376, 2.867)
	Treatment P-value [b]		0.94260
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Urinary tract infection bacterial	No. of Events (%)	13 (4.4)	3 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.967 (1.128, 13.954)
	Treatment P-value [b]		0.02040
	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.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Metabolism and nutrition disorders	No. of Events (%)	19 (6.4)	17 (5.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.028 (0.532, 1.986)
	Treatment P-value [b]		0.93546
	Homogeneity P-value [c]		NA
Musculoskeletal and connective tissue disorders	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]		0.773 (0.259, 2.308)
	Treatment P-value [b]		0.64394
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
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]		1.182 (0.581, 2.406)
	Treatment P-value [b]		0.64363
	Homogeneity P-value [c]		NA
Malignant neoplasm progression	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]		1.198 (0.516, 2.782)
	Treatment P-value [b]		0.67458
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Nervous system disorders	No. of Events (%)	13 (4.4)	4 (1.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.965 (0.966, 9.105)
	Treatment P-value [b]		0.04628
	Homogeneity P-value [c]		NA
Renal and urinary disorders	No. of Events (%)	29 (9.8)	18 (6.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.528 (0.847, 2.757)
	Treatment P-value [b]		0.15553
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Acute kidney injury	No. of Events (%)	20 (6.8)	9 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.168 (0.986, 4.766)
	Treatment P-value [b]		0.04828
	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]		1.051 (0.445, 2.480)
	Treatment P-value [b]		0.90974
	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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
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.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	44 (41.5)	46 (44.7)
	Median Survival Est. (95% CI)	NC (8.51, NC)	NC (3.48, NC)
	Hazard Ratio (95% CI) [a]		0.819 (0.542, 1.238)
	Treatment P-value [b]		0.35952
	Interaction P-value [c]		0.36240
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.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
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
Urinary tract infection bacterial	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]		0.07351
	Interaction P-value [c]		0.99058

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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=190)	Chemotherapy (N=188)
Any Event	No. of Events (%)	99 (52.1)	89 (47.3)
	Median Survival Est. (95% CI)	8.25 (4.57, NC)	NC (3.55, NC)
	Hazard Ratio (95% CI) [a]		1.034 (0.777, 1.377)
	Treatment P-value [b]		0.82180
	Interaction P-value [c]		0.36240
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.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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=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
Urinary tract infection bacterial	No. of Events (%)	9 (4.7)	3 (1.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.804 (0.758, 10.366)
	Treatment P-value [b]		0.10202
	Interaction P-value [c]		0.99058

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	118 (48.2)	107 (47.3)
	Median Survival Est. (95% CI)	14.36 (5.55, NC)	NC (3.55, NC)
	Hazard Ratio (95% CI) [a]		0.910 (0.701, 1.183)
	Treatment P-value [b]		0.50369
	Interaction P-value [c]		0.43686
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.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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
Urinary tract infection bacterial	No. of Events (%)	10 (4.1)	2 (0.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.232 (0.927, 19.328)
	Treatment P-value [b]		0.04547
	Interaction P-value [c]		0.94015

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)	28 (43.1)
	Median Survival Est. (95% CI)	NC (1.22, NC)	NC (4.07, NC)
	Hazard Ratio (95% CI) [a]		1.155 (0.673, 1.981)
	Treatment P-value [b]		0.62753
	Interaction P-value [c]		0.43686
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.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
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
Urinary tract infection bacterial	No. of Events (%)	3 (5.9)	1 (1.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.813 (0.396, 36.682)
	Treatment P-value [b]		0.18750
	Interaction P-value [c]		0.94015

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Any Event	No. of Events (%)	115 (49.1)	110 (50.2)
	Median Survival Est. (95% CI)	11.89 (5.26, NC)	7.85 (3.32, NC)
	Hazard Ratio (95% CI) [a]		0.878 (0.676, 1.140)
	Treatment P-value [b]		0.33227
	Interaction P-value [c]		0.23291
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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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
Urinary tract infection bacterial	No. of Events (%)	11 (4.7)	1 (0.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.305 (1.200, 72.151)
	Treatment P-value [b]		0.01070
	Interaction P-value [c]		0.15708

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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]		1.264 (0.737, 2.168)
	Treatment P-value [b]		0.39578
	Interaction P-value [c]		0.23291
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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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
Urinary tract infection bacterial	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]		1.201 (0.169, 8.532)
	Treatment P-value [b]		0.87283
	Interaction P-value [c]		0.15708

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	62 (50.8)	69 (56.1)
	Median Survival Est. (95% CI)	8.25 (4.07, NC)	3.32 (1.45, NC)
	Hazard Ratio (95% CI) [a]		0.755 (0.535, 1.063)
	Treatment P-value [b]		0.11320
	Interaction P-value [c]		0.04181
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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
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.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: 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]		2.039 (1.015, 4.099)
	Treatment P-value [b]		0.04107
	Interaction P-value [c]		0.04181
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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: 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

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Any Event	No. of Events (%)	58 (43.9)	54 (41.9)
	Median Survival Est. (95% CI)	NC (8.54, NC)	NC (7.72, NC)
	Hazard Ratio (95% CI) [a]		0.979 (0.675, 1.418)
	Treatment P-value [b]		0.91192
	Interaction P-value [c]		0.04181
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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: 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

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	51 (42.5)	41 (34.5)
	Median Survival Est. (95% CI)	NC (11.56, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.197 (0.793, 1.805)
	Treatment P-value [b]		0.39486
	Interaction P-value [c]		0.16344
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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
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
Urinary tract infection bacterial	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]		3.831 (0.428, 34.268)
	Treatment P-value [b]		0.20513
	Interaction P-value [c]		0.98076

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: 1

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=176)	Chemotherapy (N=172)
Any Event	No. of Events (%)	92 (52.3)	94 (54.7)
	Median Survival Est. (95% CI)	5.55 (3.32, NC)	3.48 (1.68, NC)
	Hazard Ratio (95% CI) [a]		0.838 (0.628, 1.117)
	Treatment P-value [b]		0.23620
	Interaction P-value [c]		0.16344
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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: 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
Urinary tract infection bacterial	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]		3.959 (0.854, 18.354)
	Treatment P-value [b]		0.05070
	Interaction P-value [c]		0.98076

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	51 (55.4)	46 (52.9)
	Median Survival Est. (95% CI)	4.99 (1.84, NC)	3.32 (1.45, NC)
	Hazard Ratio (95% CI) [a]		0.947 (0.636, 1.411)
	Treatment P-value [b]		0.78423
	Interaction P-value [c]		0.98393
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.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
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.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: No

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=204)	Chemotherapy (N=204)
Any Event	No. of Events (%)	92 (45.1)	89 (43.6)
	Median Survival Est. (95% CI)	NC (8.51, NC)	NC (7.72, NC)
	Hazard Ratio (95% CI) [a]		0.952 (0.711, 1.274)
	Treatment P-value [b]		0.75641
	Interaction P-value [c]		0.98393
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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: 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

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	69 (49.3)	35 (32.7)
	Median Survival Est. (95% CI)	10.45 (4.83, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.588 (1.057, 2.385)
	Treatment P-value [b]		0.01928
	Interaction P-value [c]		0.00560
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.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Urinary tract infection bacterial	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]		7.329 (0.938, 57.270)
	Treatment P-value [b]		0.02579
	Interaction P-value [c]		0.52094

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: 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)	NC (5.09, NC)	NC (1.68, NC)
	Hazard Ratio (95% CI) [a]		0.810 (0.531, 1.238)
	Treatment P-value [b]		0.35035
	Interaction P-value [c]		0.00560
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.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Docetaxel

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Urinary tract infection bacterial	No. of Events (%)	1 (1.2)	1 (0.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.131 (0.071, 18.110)
	Treatment P-value [b]		0.85516
	Interaction P-value [c]		0.52094

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	37 (52.1)	49 (65.3)
	Median Survival Est. (95% CI)	8.51 (1.84, NC)	1.94 (0.56, 6.60)
	Hazard Ratio (95% CI) [a]		0.624 (0.407, 0.957)
	Treatment P-value [b]		0.02996
	Interaction P-value [c]		0.00560
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.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Urinary tract infection bacterial	No. of Events (%)	2 (2.8)	1 (1.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.015 (0.183, 22.232)
	Treatment P-value [b]		0.57074
	Interaction P-value [c]		0.52094

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Any Event	No. of Events (%)	42 (43.8)	41 (40.2)
	Median Survival Est. (95% CI)	NC (8.15, NC)	NC (9.86, NC)
	Hazard Ratio (95% CI) [a]		1.002 (0.652, 1.541)
	Treatment P-value [b]		0.99731
	Interaction P-value [c]		0.76998
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.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: 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
Urinary tract infection bacterial	No. of Events (%)	2 (2.1)	1 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.020 (0.183, 22.281)
	Treatment P-value [b]		0.53657
	Interaction P-value [c]		0.55077

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	101 (50.5)	94 (49.7)
	Median Survival Est. (95% CI)	8.51 (4.07, NC)	7.72 (3.09, NC)
	Hazard Ratio (95% CI) [a]		0.928 (0.701, 1.229)
	Treatment P-value [b]		0.61836
	Interaction P-value [c]		0.76998
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.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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
Urinary tract infection bacterial	No. of Events (%)	11 (5.5)	2 (1.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.786 (1.060, 21.616)
	Treatment P-value [b]		0.02455
	Interaction P-value [c]		0.55077

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
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.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	124 (47.9)	118 (46.3)
	Median Survival Est. (95% CI)	NC (5.26, NC)	NC (5.26, NC)
	Hazard Ratio (95% CI) [a]		0.957 (0.744, 1.231)
	Treatment P-value [b]		0.72783
	Interaction P-value [c]		0.97569
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.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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
Urinary tract infection bacterial	No. of Events (%)	10 (3.9)	2 (0.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.575 (1.002, 20.897)
	Treatment P-value [b]		0.03182
	Interaction P-value [c]		0.71989

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	19 (51.4)	17 (47.2)
	Median Survival Est. (95% CI)	14.36 (3.71, NC)	NC (1.35, NC)
	Hazard Ratio (95% CI) [a]		0.946 (0.492, 1.821)
	Treatment P-value [b]		0.87496
	Interaction P-value [c]		0.97569
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.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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
Urinary tract infection bacterial	No. of Events (%)	3 (8.1)	1 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.778 (0.289, 26.722)
	Treatment P-value [b]		0.36891
	Interaction P-value [c]		0.71989

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Any Event	No. of Events (%)	28 (45.9)	26 (53.1)
	Median Survival Est. (95% CI)	NC (4.60, NC)	3.58 (1.41, NC)
	Hazard Ratio (95% CI) [a]		0.725 (0.425, 1.237)
	Treatment P-value [b]		0.25463
	Interaction P-value [c]		0.14668
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.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: 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
Urinary tract infection bacterial	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]		0.14164
	Interaction P-value [c]		0.99277

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: 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.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Any Event	No. of Events (%)	101 (50.0)	86 (42.6)
	Median Survival Est. (95% CI)	11.53 (4.83, NC)	NC (9.86, NC)
	Hazard Ratio (95% CI) [a]		1.137 (0.852, 1.515)
	Treatment P-value [b]		0.38503
	Interaction P-value [c]		0.14668
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.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
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
Urinary tract infection bacterial	No. of Events (%)	10 (5.0)	3 (1.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.167 (0.871, 11.515)
	Treatment P-value [b]		0.06272
	Interaction P-value [c]		0.99277

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

3.8 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 (%)	42 (39.6)	42 (40.8)
	Median Survival Est. (95% CI)	NC (11.53, NC)	NC (4.47, NC)
	Hazard Ratio (95% CI) [a]		0.855 (0.558, 1.312)
	Treatment P-value [b]		0.49766
	Interaction P-value [c]		0.50529

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	93 (48.9)	85 (45.2)
	Median Survival Est. (95% CI)	14.36 (4.83, NC)	NC (4.07, NC)
	Hazard Ratio (95% CI) [a]		1.020 (0.760, 1.369)
	Treatment P-value [b]		0.90280
	Interaction P-value [c]		0.50529

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	110 (44.9)	101 (44.7)
	Median Survival Est. (95% CI)	NC (8.51, NC)	NC (4.44, NC)
	Hazard Ratio (95% CI) [a]		0.902 (0.689, 1.182)
	Treatment P-value [b]		0.47416
	Interaction P-value [c]		0.31241

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)	26 (40.0)
	Median Survival Est. (95% CI)	NC (1.45, NC)	NC (4.07, NC)
	Hazard Ratio (95% CI) [a]		1.237 (0.714, 2.142)
	Treatment P-value [b]		0.47670
	Interaction P-value [c]		0.31241

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	108 (46.2)	102 (46.6)
	Median Survival Est. (95% CI)	NC (8.15, NC)	NC (3.81, NC)
	Hazard Ratio (95% CI) [a]		0.891 (0.680, 1.168)
	Treatment P-value [b]		0.40722
	Interaction P-value [c]		0.31388

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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]		1.217 (0.707, 2.097)
	Treatment P-value [b]		0.47915
	Interaction P-value [c]		0.31388

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	57 (46.7)	64 (52.0)
	Median Survival Est. (95% CI)	11.89 (4.83, NC)	3.48 (2.10, NC)
	Hazard Ratio (95% CI) [a]		0.750 (0.525, 1.072)
	Treatment P-value [b]		0.11509
	Interaction P-value [c]		0.02738

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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]		2.248 (1.096, 4.613)
	Treatment P-value [b]		0.02350
	Interaction P-value [c]		0.02738

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	55 (41.7)	52 (40.3)
	Median Survival Est. (95% CI)	NC (14.36, NC)	NC (7.85, NC)
	Hazard Ratio (95% CI) [a]		0.961 (0.658, 1.404)
	Treatment P-value [b]		0.83888
	Interaction P-value [c]		0.02738

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	48 (40.0)	40 (33.6)
	Median Survival Est. (95% CI)	NC (14.36, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.151 (0.757, 1.751)
	Treatment P-value [b]		0.51291
	Interaction P-value [c]		0.26698

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	87 (49.4)	87 (50.6)
	Median Survival Est. (95% CI)	8.41 (3.55, NC)	5.26 (2.10, NC)
	Hazard Ratio (95% CI) [a]		0.860 (0.639, 1.158)
	Treatment P-value [b]		0.33277
	Interaction P-value [c]		0.26698

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	46 (50.0)	43 (49.4)
	Median Survival Est. (95% CI)	8.25 (2.14, NC)	18.00 (1.45, NC)
	Hazard Ratio (95% CI) [a]		0.905 (0.597, 1.371)
	Treatment P-value [b]		0.63945
	Interaction P-value [c]		0.75635

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	89 (43.6)	84 (41.2)
	Median Survival Est. (95% CI)	NC (10.45, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.981 (0.728, 1.322)
	Treatment P-value [b]		0.91569
	Interaction P-value [c]		0.75635

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	67 (47.9)	31 (29.0)
	Median Survival Est. (95% CI)	14.36 (4.99, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.735 (1.133, 2.655)
	Treatment P-value [b]		0.00809
	Interaction P-value [c]		0.00161

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)	NC (5.09, NC)	NC (2.63, NC)
	Hazard Ratio (95% CI) [a]		0.803 (0.520, 1.239)
	Treatment P-value [b]		0.34305
	Interaction P-value [c]		0.00161

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Vinflunine

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Any Event	No. of Events (%)	33 (46.5)	47 (62.7)
	Median Survival Est. (95% CI)	NC (3.55, NC)	2.27 (0.79, 7.85)
	Hazard Ratio (95% CI) [a]		0.583 (0.374, 0.911)
	Treatment P-value [b]		0.01738
	Interaction P-value [c]		0.00161

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)	39 (38.2)
	Median Survival Est. (95% CI)	NC (10.45, NC)	NC (18.00, NC)
	Hazard Ratio (95% CI) [a]		0.970 (0.622, 1.512)
	Treatment P-value [b]		0.89528
	Interaction P-value [c]		0.93323

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	96 (48.0)	88 (46.6)
	Median Survival Est. (95% CI)	18.17 (4.83, NC)	NC (3.81, NC)
	Hazard Ratio (95% CI) [a]		0.949 (0.710, 1.267)
	Treatment P-value [b]		0.72914
	Interaction P-value [c]		0.93323

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	117 (45.2)	111 (43.5)
	Median Survival Est. (95% CI)	NC (8.25, NC)	NC (7.72, NC)
	Hazard Ratio (95% CI) [a]		0.962 (0.742, 1.248)
	Treatment P-value [b]		0.76682
	Interaction P-value [c]		0.95638

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	18 (48.6)	16 (44.4)
	Median Survival Est. (95% CI)	18.17 (3.71, NC)	NC (1.35, NC)
	Hazard Ratio (95% CI) [a]		0.943 (0.481, 1.850)
	Treatment P-value [b]		0.87669
	Interaction P-value [c]		0.95638

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	27 (44.3)	24 (49.0)
	Median Survival Est. (95% CI)	NC (4.60, NC)	7.72 (1.41, NC)
	Hazard Ratio (95% CI) [a]		0.758 (0.437, 1.314)
	Treatment P-value [b]		0.34435
	Interaction P-value [c]		0.20396

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	96 (47.5)	82 (40.6)
	Median Survival Est. (95% CI)	18.17 (5.26, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.136 (0.846, 1.525)
	Treatment P-value [b]		0.39629
	Interaction P-value [c]		0.20396

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

3.9 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 (%)	16 (15.1)	21 (20.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.645 (0.336, 1.236)
	Treatment P-value [b]		0.16619
	Interaction P-value [c]		0.19923

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	46 (24.2)	40 (21.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.072 (0.702, 1.639)
	Treatment P-value [b]		0.73500
	Interaction P-value [c]		0.19923

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	46 (18.8)	47 (20.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.811 (0.540, 1.219)
	Treatment P-value [b]		0.30056
	Interaction P-value [c]		0.16765

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	16 (31.4)	14 (21.5)
	Median Survival Est. (95% CI)	NC (20.11, NC)	NC (24.87, NC)
	Hazard Ratio (95% CI) [a]		1.450 (0.707, 2.971)
	Treatment P-value [b]		0.30581
	Interaction P-value [c]		0.16765

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	52 (22.2)	44 (20.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.993 (0.664, 1.485)
	Treatment P-value [b]		0.99960
	Interaction P-value [c]		0.37450

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	10 (16.1)	17 (23.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (24.87, NC)
	Hazard Ratio (95% CI) [a]		0.667 (0.305, 1.457)
	Treatment P-value [b]		0.33213
	Interaction P-value [c]		0.37450

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Western Europe

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Any Event	No. of Events (%)	33 (27.0)	31 (25.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.974 (0.597, 1.591)
	Treatment P-value [b]		0.89969
	Interaction P-value [c]		0.05240

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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]		7.913 (0.990, 63.274)
	Treatment P-value [b]		0.02255
	Interaction P-value [c]		0.05240

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Rest of the World

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=132)	Chemotherapy (N=129)
Any Event	No. of Events (%)	21 (15.9)	29 (22.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (24.87, NC)
	Hazard Ratio (95% CI) [a]		0.622 (0.355, 1.092)
	Treatment P-value [b]		0.09396
	Interaction P-value [c]		0.05240

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	26 (21.7)	22 (18.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.133 (0.642, 1.999)
	Treatment P-value [b]		0.65907
	Interaction P-value [c]		0.33195

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	36 (20.5)	39 (22.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.791 (0.502, 1.244)
	Treatment P-value [b]		0.32057
	Interaction P-value [c]		0.33195

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Yes

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=92)	Chemotherapy (N=87)
Any Event	No. of Events (%)	27 (29.3)	16 (18.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.495 (0.805, 2.777)
	Treatment P-value [b]		0.16788
	Interaction P-value [c]		0.05204

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	35 (17.2)	45 (22.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.704 (0.452, 1.095)
	Treatment P-value [b]		0.11753
	Interaction P-value [c]		0.05204

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	19 (13.6)	20 (18.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.656 (0.350, 1.229)
	Treatment P-value [b]		0.15267
	Interaction P-value [c]		0.30135

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	18 (21.2)	21 (19.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (24.87, NC)
	Hazard Ratio (95% CI) [a]		0.987 (0.526, 1.854)
	Treatment P-value [b]		0.98088
	Interaction P-value [c]		0.30135

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	25 (35.2)	20 (26.7)
	Median Survival Est. (95% CI)	NC (11.53, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.292 (0.718, 2.326)
	Treatment P-value [b]		0.41999
	Interaction P-value [c]		0.30135

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Upper Tract

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Any Event	No. of Events (%)	22 (22.9)	24 (23.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (24.87, NC)
	Hazard Ratio (95% CI) [a]		0.902 (0.506, 1.610)
	Treatment P-value [b]		0.69940
	Interaction P-value [c]		0.93489

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	40 (20.0)	37 (19.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.930 (0.595, 1.455)
	Treatment P-value [b]		0.77800
	Interaction P-value [c]		0.93489

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: 1-2 lines

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=259)	Chemotherapy (N=255)
Any Event	No. of Events (%)	55 (21.2)	54 (21.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.919 (0.631, 1.339)
	Treatment P-value [b]		0.65265
	Interaction P-value [c]		0.95151

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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]		0.888 (0.311, 2.532)
	Treatment P-value [b]		0.80349
	Interaction P-value [c]		0.95151

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	15 (24.6)	9 (18.4)
	Median Survival Est. (95% CI)	NC (20.70, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.218 (0.533, 2.786)
	Treatment P-value [b]		0.56998
	Interaction P-value [c]		0.53369

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Non-responder

System Organ Class Preferred Term	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Any Event	No. of Events (%)	41 (20.3)	42 (20.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.906 (0.589, 1.394)
	Treatment P-value [b]		0.64665
	Interaction P-value [c]		0.53369

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_AE_KM.SAS
Date/time of run: 06DEC2021 17:06. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

3.10 Subgruppenanalysen zu den unerwünschten Ereignissen von besonderem Interesse

3.10.1 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)
Any	No. of Events (%)	78 (73.6)	55 (53.4)
	Median Survival Est. (95% CI)	1.02 (0.72, 2.20)	3.71 (2.10, NC)
	Hazard Ratio (95% CI) [a]		1.678 (1.188, 2.370)
	Treatment P-value [b]		0.00309
	Interaction P-value [c]		0.28530
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]		3.831 (0.813, 18.040)
	Treatment P-value [b]		0.06744
	Interaction P-value [c]		0.91903

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	9 (8.5)	8 (7.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.036 (0.400, 2.687)
	Treatment P-value [b]		0.95470
	Interaction P-value [c]		0.50071
Ocular 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]		3.262 (1.400, 7.602)
	Treatment P-value [b]		0.00385
	Interaction P-value [c]		0.57923

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Peripheral Neuropathy	No. of Events (%)	53 (50.0)	36 (35.0)
	Median Survival Est. (95% CI)	6.93 (5.13, NC)	NC (9.07, NC)
	Hazard Ratio (95% CI) [a]		1.313 (0.860, 2.004)
	Treatment P-value [b]		0.20399
	Interaction P-value [c]		0.60130
Skin reactions	No. of Events (%)	57 (53.8)	23 (22.3)
	Median Survival Est. (95% CI)	6.60 (1.35, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.076 (1.895, 4.994)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.99565

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Any	No. of Events (%)	153 (80.5)	99 (52.7)
	Median Survival Est. (95% CI)	0.85 (0.59, 1.15)	3.45 (2.27, 12.29)
	Hazard Ratio (95% CI) [a]		2.119 (1.642, 2.733)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.28530
Hyperglycemia	No. of Events (%)	27 (14.2)	8 (4.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.500 (1.590, 7.708)
	Treatment P-value [b]		0.00104
	Interaction P-value [c]		0.91903

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Infusion related reaction	No. of Events (%)	19 (10.0)	12 (6.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.563 (0.758, 3.220)
	Treatment P-value [b]		0.21419
	Interaction P-value [c]		0.50071
Ocular disorders	No. of Events (%)	64 (33.7)	17 (9.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.330 (2.536, 7.393)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.57923

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Peripheral Neuropathy	No. of Events (%)	100 (52.6)	68 (36.2)
	Median Survival Est. (95% CI)	4.86 (4.04, 7.92)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.509 (1.109, 2.055)
	Treatment P-value [b]		0.00929
	Interaction P-value [c]		0.60130
Skin reactions	No. of Events (%)	106 (55.8)	44 (23.4)
	Median Survival Est. (95% CI)	2.33 (1.05, 7.95)	NC (28.32, NC)
	Hazard Ratio (95% CI) [a]		3.081 (2.167, 4.382)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.99565

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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=245)	Chemotherapy (N=226)
Any	No. of Events (%)	190 (77.6)	119 (52.7)
	Median Survival Est. (95% CI)	0.92 (0.72, 1.28)	3.68 (2.33, 7.33)
	Hazard Ratio (95% CI) [a]		1.940 (1.541, 2.442)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.97886
Hyperglycemia	No. of Events (%)	25 (10.2)	7 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.310 (1.431, 7.655)
	Treatment P-value [b]		0.00288
	Interaction P-value [c]		0.64918

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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=245)	Chemotherapy (N=226)
Infusion related reaction	No. of Events (%)	28 (11.4)	12 (5.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.123 (1.079, 4.176)
	Treatment P-value [b]		0.02522
	Interaction P-value [c]		0.98581
Ocular disorders	No. of Events (%)	67 (27.3)	16 (7.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.162 (2.412, 7.181)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.95200

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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=245)	Chemotherapy (N=226)
Peripheral Neuropathy	No. of Events (%)	130 (53.1)	82 (36.3)
	Median Survival Est. (95% CI)	5.32 (4.60, 8.31)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.429 (1.084, 1.885)
	Treatment P-value [b]		0.00981
	Interaction P-value [c]		0.90016
Skin reactions	No. of Events (%)	136 (55.5)	52 (23.0)
	Median Survival Est. (95% CI)	3.35 (1.35, 8.08)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.124 (2.268, 4.303)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.78744

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Any	No. of Events (%)	41 (80.4)	35 (53.8)
	Median Survival Est. (95% CI)	0.95 (0.46, 1.61)	3.29 (0.89, NC)
	Hazard Ratio (95% CI) [a]		1.953 (1.243, 3.069)
	Treatment P-value [b]		0.00458
	Interaction P-value [c]		0.97886
Hyperglycemia	No. of Events (%)	10 (19.6)	3 (4.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.731 (1.302, 17.195)
	Treatment P-value [b]		0.01115
	Interaction P-value [c]		0.64918

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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	8 (12.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.01010
	Interaction P-value [c]		0.98581
Ocular disorders	No. of Events (%)	20 (39.2)	8 (12.3)
	Median Survival Est. (95% CI)	NC (3.94, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.038 (1.778, 9.173)
	Treatment P-value [b]		0.00050
	Interaction P-value [c]		0.95200

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Peripheral 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]		1.371 (0.764, 2.461)
	Treatment P-value [b]		0.31587
	Interaction P-value [c]		0.90016
Skin reactions	No. of Events (%)	27 (52.9)	15 (23.1)
	Median Survival Est. (95% CI)	2.79 (0.59, NC)	28.32 (22.83, NC)
	Hazard Ratio (95% CI) [a]		2.834 (1.506, 5.333)
	Treatment P-value [b]		0.00093
	Interaction P-value [c]		0.78744

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Any	No. of Events (%)	189 (80.8)	111 (50.7)
	Median Survival Est. (95% CI)	0.92 (0.62, 1.05)	3.94 (2.40, NC)
	Hazard Ratio (95% CI) [a]		2.201 (1.738, 2.786)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.02886
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]		5.071 (2.119, 12.132)
	Treatment P-value [b]		0.00004
	Interaction P-value [c]		0.05237

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Infusion related reaction	No. of Events (%)	20 (8.5)	15 (6.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.194 (0.611, 2.333)
	Treatment P-value [b]		0.60778
	Interaction P-value [c]		0.45204
Ocular disorders	No. of Events (%)	72 (30.8)	17 (7.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.344 (2.560, 7.371)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.42042

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Peripheral Neuropathy	No. of Events (%)	126 (53.8)	75 (34.2)
	Median Survival Est. (95% CI)	5.13 (4.21, 8.31)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.590 (1.195, 2.117)
	Treatment P-value [b]		0.00124
	Interaction P-value [c]		0.12683
Skin reactions	No. of Events (%)	130 (55.6)	45 (20.5)
	Median Survival Est. (95% CI)	3.35 (1.35, 10.84)	NC (28.32, NC)
	Hazard Ratio (95% CI) [a]		3.503 (2.494, 4.920)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.15066

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Any	No. of Events (%)	42 (67.7)	43 (59.7)
	Median Survival Est. (95% CI)	1.28 (0.59, 2.33)	2.73 (0.79, 6.51)
	Hazard Ratio (95% CI) [a]		1.280 (0.837, 1.959)
	Treatment P-value [b]		0.28385
	Interaction P-value [c]		0.02886
Hyperglycemia	No. of Events (%)	3 (4.8)	4 (5.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.912 (0.204, 4.077)
	Treatment P-value [b]		0.94255
	Interaction P-value [c]		0.05237

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)	5 (6.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.968 (0.644, 6.017)
	Treatment P-value [b]		0.23482
	Interaction P-value [c]		0.45204
Ocular disorders	No. of Events (%)	15 (24.2)	7 (9.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.831 (1.154, 6.945)
	Treatment P-value [b]		0.01444
	Interaction P-value [c]		0.42042

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Peripheral Neuropathy	No. of Events (%)	27 (43.5)	29 (40.3)
	Median Survival Est. (95% CI)	6.93 (4.63, NC)	NC (5.26, NC)
	Hazard Ratio (95% CI) [a]		0.999 (0.591, 1.688)
	Treatment P-value [b]		0.99126
	Interaction P-value [c]		0.12683
Skin reactions	No. of Events (%)	33 (53.2)	22 (30.6)
	Median Survival Est. (95% CI)	2.73 (0.92, NC)	NC (17.68, NC)
	Hazard Ratio (95% CI) [a]		2.194 (1.278, 3.766)
	Treatment P-value [b]		0.00231
	Interaction P-value [c]		0.15066

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Any	No. of Events (%)	90 (73.8)	53 (43.1)
	Median Survival Est. (95% CI)	1.22 (0.89, 2.07)	12.29 (5.26, NC)
	Hazard Ratio (95% CI) [a]		2.156 (1.533, 3.032)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.46220
Hyperglycemia	No. of Events (%)	16 (13.1)	6 (4.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.642 (1.034, 6.754)
	Treatment P-value [b]		0.03414
	Interaction P-value [c]		0.99807

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	6 (4.9)	8 (6.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.702 (0.244, 2.024)
	Treatment P-value [b]		0.52137
	Interaction P-value [c]		0.22861
Ocular disorders	No. of Events (%)	50 (41.0)	6 (4.9)
	Median Survival Est. (95% CI)	NC (6.05, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		10.261 (4.397, 23.944)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.00480

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Peripheral Neuropathy	No. of Events (%)	64 (52.5)	32 (26.0)
	Median Survival Est. (95% CI)	5.78 (3.29, 8.80)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.264 (1.481, 3.463)
	Treatment P-value [b]		0.00012
	Interaction P-value [c]		0.01607
Skin reactions	No. of Events (%)	59 (48.4)	19 (15.4)
	Median Survival Est. (95% CI)	10.84 (3.35, NC)	NC (28.32, NC)
	Hazard Ratio (95% CI) [a]		3.648 (2.175, 6.118)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.68896

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Any	No. of Events (%)	35 (83.3)	22 (56.4)
	Median Survival Est. (95% CI)	0.72 (0.43, 1.18)	3.78 (2.27, NC)
	Hazard Ratio (95% CI) [a]		2.331 (1.366, 3.978)
	Treatment P-value [b]		0.00061
	Interaction P-value [c]		0.46220
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]		0.99807

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
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]		4.970 (0.581, 42.547)
	Treatment P-value [b]		0.10269
	Interaction P-value [c]		0.22861
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]		1.460 (0.624, 3.417)
	Treatment P-value [b]		0.36337
	Interaction P-value [c]		0.00480

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Peripheral 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]		1.376 (0.727, 2.604)
	Treatment P-value [b]		0.32225
	Interaction P-value [c]		0.01607
Skin reactions	No. of Events (%)	26 (61.9)	10 (25.6)
	Median Survival Est. (95% CI)	1.23 (0.49, NC)	NC (8.97, NC)
	Hazard Ratio (95% CI) [a]		3.402 (1.639, 7.059)
	Treatment P-value [b]		0.00030
	Interaction P-value [c]		0.68896

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Any	No. of Events (%)	106 (80.3)	79 (61.2)
	Median Survival Est. (95% CI)	0.72 (0.49, 1.18)	2.14 (1.38, 2.83)
	Hazard Ratio (95% CI) [a]		1.710 (1.277, 2.290)
	Treatment P-value [b]		0.00036
	Interaction P-value [c]		0.46220
Hyperglycemia	No. of Events (%)	11 (8.3)	4 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.762 (0.879, 8.678)
	Treatment P-value [b]		0.07517
	Interaction P-value [c]		0.99807

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)	11 (8.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.512 (0.708, 3.230)
	Treatment P-value [b]		0.28282
	Interaction P-value [c]		0.22861
Ocular disorders	No. of Events (%)	24 (18.2)	9 (7.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.693 (1.251, 5.794)
	Treatment P-value [b]		0.00922
	Interaction P-value [c]		0.00480

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Peripheral Neuropathy	No. of Events (%)	66 (50.0)	56 (43.4)
	Median Survival Est. (95% CI)	6.34 (4.83, NC)	NC (3.68, NC)
	Hazard Ratio (95% CI) [a]		1.004 (0.703, 1.434)
	Treatment P-value [b]		0.97631
	Interaction P-value [c]		0.01607
Skin reactions	No. of Events (%)	78 (59.1)	38 (29.5)
	Median Survival Est. (95% CI)	1.35 (0.62, 5.98)	NC (22.83, NC)
	Hazard Ratio (95% CI) [a]		2.780 (1.885, 4.099)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.68896

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Any	No. of Events (%)	101 (84.2)	72 (60.5)
	Median Survival Est. (95% CI)	0.53 (0.43, 0.92)	2.37 (1.64, 5.26)
	Hazard Ratio (95% CI) [a]		2.129 (1.570, 2.886)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.52818
Hyperglycemia	No. of Events (%)	12 (10.0)	4 (3.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.103 (1.001, 9.621)
	Treatment P-value [b]		0.03835
	Interaction P-value [c]		0.78789

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Infusion related reaction	No. of Events (%)	18 (15.0)	9 (7.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.045 (0.919, 4.553)
	Treatment P-value [b]		0.07523
	Interaction P-value [c]		0.13630
Ocular disorders	No. of Events (%)	36 (30.0)	8 (6.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.152 (2.395, 11.082)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.36729

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Peripheral Neuropathy	No. of Events (%)	70 (58.3)	49 (41.2)
	Median Survival Est. (95% CI)	4.96 (3.71, 8.80)	NC (6.57, NC)
	Hazard Ratio (95% CI) [a]		1.459 (1.013, 2.104)
	Treatment P-value [b]		0.04311
	Interaction P-value [c]		0.90550
Skin reactions	No. of Events (%)	78 (65.0)	33 (27.7)
	Median Survival Est. (95% CI)	0.87 (0.49, 3.35)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.567 (2.371, 5.367)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.42416

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Any	No. of Events (%)	130 (73.9)	82 (47.7)
	Median Survival Est. (95% CI)	1.28 (0.95, 1.91)	5.82 (2.79, NC)
	Hazard Ratio (95% CI) [a]		1.865 (1.414, 2.461)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.52818
Hyperglycemia	No. of Events (%)	23 (13.1)	6 (3.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.783 (1.540, 9.296)
	Treatment P-value [b]		0.00181
	Interaction P-value [c]		0.78789

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	10 (5.7)	11 (6.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.839 (0.356, 1.977)
	Treatment P-value [b]		0.69847
	Interaction P-value [c]		0.13630
Ocular disorders	No. of Events (%)	51 (29.0)	16 (9.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.328 (1.898, 5.837)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.36729

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Peripheral Neuropathy	No. of Events (%)	83 (47.2)	55 (32.0)
	Median Survival Est. (95% CI)	6.93 (4.60, 10.84)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.416 (1.007, 1.991)
	Treatment P-value [b]		0.04393
	Interaction P-value [c]		0.90550
Skin reactions	No. of Events (%)	85 (48.3)	34 (19.8)
	Median Survival Est. (95% CI)	8.08 (2.33, NC)	28.32 (22.83, NC)
	Hazard Ratio (95% CI) [a]		2.827 (1.898, 4.210)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.42416

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Any	No. of Events (%)	67 (72.8)	40 (46.0)
	Median Survival Est. (95% CI)	0.92 (0.59, 1.38)	5.49 (2.76, NC)
	Hazard Ratio (95% CI) [a]		2.220 (1.500, 3.288)
	Treatment P-value [b]		0.00005
	Interaction P-value [c]		0.42822
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]		9.783 (1.253, 76.393)
	Treatment P-value [b]		0.00684
	Interaction P-value [c]		0.26766

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)	3 (3.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.867 (0.467, 7.468)
	Treatment P-value [b]		0.39604
	Interaction P-value [c]		0.61554
Ocular disorders	No. of Events (%)	24 (26.1)	8 (9.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.079 (1.383, 6.856)
	Treatment P-value [b]		0.00399
	Interaction P-value [c]		0.47550

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Peripheral 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]		1.241 (0.773, 1.992)
	Treatment P-value [b]		0.36475
	Interaction P-value [c]		0.48229
Skin reactions	No. of Events (%)	51 (55.4)	16 (18.4)
	Median Survival Est. (95% CI)	2.17 (0.92, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.910 (2.228, 6.861)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.32291

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Any	No. of Events (%)	164 (80.4)	114 (55.9)
	Median Survival Est. (95% CI)	0.95 (0.69, 1.35)	2.83 (1.87, 5.88)
	Hazard Ratio (95% CI) [a]		1.844 (1.451, 2.345)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.42822
Hyperglycemia	No. of Events (%)	25 (12.3)	9 (4.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.832 (1.322, 6.068)
	Treatment P-value [b]		0.00522
	Interaction P-value [c]		0.26766

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	22 (10.8)	17 (8.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.264 (0.671, 2.380)
	Treatment P-value [b]		0.45740
	Interaction P-value [c]		0.61554
Ocular disorders	No. of Events (%)	63 (30.9)	16 (7.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.384 (2.532, 7.590)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.47550

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Peripheral Neuropathy	No. of Events (%)	113 (55.4)	74 (36.3)
	Median Survival Est. (95% CI)	5.68 (4.60, 8.34)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.515 (1.129, 2.031)
	Treatment P-value [b]		0.00474
	Interaction P-value [c]		0.48229
Skin reactions	No. of Events (%)	112 (54.9)	51 (25.0)
	Median Survival Est. (95% CI)	4.11 (1.41, 14.55)	NC (28.32, NC)
	Hazard Ratio (95% CI) [a]		2.814 (2.020, 3.920)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.32291

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Paclitaxel

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Any	No. of Events (%)	107 (76.4)	69 (64.5)
	Median Survival Est. (95% CI)	0.95 (0.59, 1.51)	1.15 (0.72, 2.33)
	Hazard Ratio (95% CI) [a]		1.246 (0.921, 1.686)
	Treatment P-value [b]		0.15272
	Interaction P-value [c]		0.00166
Hyperglycemia	No. of Events (%)	14 (10.0)	3 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.634 (1.044, 12.646)
	Treatment P-value [b]		0.03104
	Interaction P-value [c]		0.31941

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Paclitaxel

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Infusion related reaction	No. of Events (%)	14 (10.0)	7 (6.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.491 (0.602, 3.696)
	Treatment P-value [b]		0.39534
	Interaction P-value [c]		0.45673
Ocular disorders	No. of Events (%)	33 (23.6)	7 (6.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.877 (1.715, 8.765)
	Treatment P-value [b]		0.00042
	Interaction P-value [c]		0.01953

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Paclitaxel

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Peripheral Neuropathy	No. of Events (%)	75 (53.6)	60 (56.1)
	Median Survival Est. (95% CI)	5.06 (4.21, 7.62)	2.79 (1.48, 7.43)
	Hazard Ratio (95% CI) [a]		0.695 (0.495, 0.977)
	Treatment P-value [b]		0.04091
	Interaction P-value [c]		<.00001
Skin reactions	No. of Events (%)	76 (54.3)	28 (26.2)
	Median Survival Est. (95% CI)	4.11 (1.31, NC)	28.32 (28.32, NC)
	Hazard Ratio (95% CI) [a]		2.612 (1.693, 4.029)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.51460

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Docetaxel

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Any	No. of Events (%)	69 (81.2)	56 (51.4)
	Median Survival Est. (95% CI)	0.72 (0.43, 1.18)	4.60 (2.43, NC)
	Hazard Ratio (95% CI) [a]		2.445 (1.717, 3.482)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.00166
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]		7.991 (1.788, 35.711)
	Treatment P-value [b]		0.00111
	Interaction P-value [c]		0.31941

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: 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]		1.832 (0.697, 4.816)
	Treatment P-value [b]		0.18296
	Interaction P-value [c]		0.45673
Ocular disorders	No. of Events (%)	23 (27.1)	14 (12.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.133 (1.098, 4.147)
	Treatment P-value [b]		0.02297
	Interaction P-value [c]		0.01953

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Docetaxel

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Peripheral Neuropathy	No. of Events (%)	42 (49.4)	30 (27.5)
	Median Survival Est. (95% CI)	8.31 (4.21, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.862 (1.165, 2.974)
	Treatment P-value [b]		0.00793
	Interaction P-value [c]		<.00001
Skin reactions	No. of Events (%)	52 (61.2)	28 (25.7)
	Median Survival Est. (95% CI)	1.41 (0.49, 5.98)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.381 (2.134, 5.357)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.51460

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Any	No. of Events (%)	55 (77.5)	29 (38.7)
	Median Survival Est. (95% CI)	1.02 (0.72, 1.87)	NC (6.51, NC)
	Hazard Ratio (95% CI) [a]		2.916 (1.855, 4.582)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.00166
Hyperglycemia	No. of Events (%)	9 (12.7)	5 (6.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.933 (0.648, 5.769)
	Treatment P-value [b]		0.22893
	Interaction P-value [c]		0.31941

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Infusion related reaction	No. of Events (%)	4 (5.6)	6 (8.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.678 (0.191, 2.404)
	Treatment P-value [b]		0.53076
	Interaction P-value [c]		0.45673
Ocular disorders	No. of Events (%)	31 (43.7)	3 (4.0)
	Median Survival Est. (95% CI)	9.95 (3.29, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		14.807 (4.524, 48.463)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.01953

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Peripheral Neuropathy	No. of Events (%)	36 (50.7)	14 (18.7)
	Median Survival Est. (95% CI)	5.78 (2.89, 10.84)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.547 (1.912, 6.581)
	Treatment P-value [b]		0.00002
	Interaction P-value [c]		<.00001
Skin reactions	No. of Events (%)	35 (49.3)	11 (14.7)
	Median Survival Est. (95% CI)	8.08 (2.17, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.045 (2.054, 7.968)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.51460

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Any	No. of Events (%)	80 (83.3)	56 (54.9)
	Median Survival Est. (95% CI)	0.72 (0.49, 1.28)	3.45 (1.41, NC)
	Hazard Ratio (95% CI) [a]		2.067 (1.467, 2.912)
	Treatment P-value [b]		0.00003
	Interaction P-value [c]		0.69600
Hyperglycemia	No. of Events (%)	12 (12.5)	7 (6.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.860 (0.732, 4.724)
	Treatment P-value [b]		0.20336
	Interaction P-value [c]		0.07412

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)	6 (5.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.401 (0.486, 4.039)
	Treatment P-value [b]		0.54379
	Interaction P-value [c]		0.91951
Ocular disorders	No. of Events (%)	25 (26.0)	7 (6.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.049 (1.751, 9.361)
	Treatment P-value [b]		0.00044
	Interaction P-value [c]		0.93508

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Peripheral Neuropathy	No. of Events (%)	52 (54.2)	38 (37.3)
	Median Survival Est. (95% CI)	5.13 (3.75, 8.31)	NC (5.26, NC)
	Hazard Ratio (95% CI) [a]		1.428 (0.939, 2.170)
	Treatment P-value [b]		0.09573
	Interaction P-value [c]		0.97470
Skin reactions	No. of Events (%)	60 (62.5)	25 (24.5)
	Median Survival Est. (95% CI)	1.31 (0.59, 3.78)	NC (22.83, NC)
	Hazard Ratio (95% CI) [a]		3.517 (2.203, 5.613)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.51846

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Any	No. of Events (%)	151 (75.5)	98 (51.9)
	Median Survival Est. (95% CI)	0.99 (0.76, 1.41)	3.94 (2.33, NC)
	Hazard Ratio (95% CI) [a]		1.898 (1.471, 2.450)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.69600
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]		7.442 (2.234, 24.788)
	Treatment P-value [b]		0.00010
	Interaction P-value [c]		0.07412

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	20 (10.0)	14 (7.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.313 (0.663, 2.601)
	Treatment P-value [b]		0.42200
	Interaction P-value [c]		0.91951
Ocular disorders	No. of Events (%)	62 (31.0)	17 (9.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.885 (2.271, 6.644)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.93508

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Peripheral Neuropathy	No. of Events (%)	101 (50.5)	66 (34.9)
	Median Survival Est. (95% CI)	6.60 (4.40, 10.84)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.440 (1.056, 1.964)
	Treatment P-value [b]		0.01993
	Interaction P-value [c]		0.97470
Skin reactions	No. of Events (%)	103 (51.5)	42 (22.2)
	Median Survival Est. (95% CI)	7.06 (2.17, NC)	28.32 (28.32, NC)
	Hazard Ratio (95% CI) [a]		2.896 (2.022, 4.148)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.51846

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Any	No. of Events (%)	204 (78.8)	132 (51.8)
	Median Survival Est. (95% CI)	0.95 (0.72, 1.31)	3.78 (2.43, 9.03)
	Hazard Ratio (95% CI) [a]		2.028 (1.627, 2.528)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.27235
Hyperglycemia	No. of Events (%)	32 (12.4)	10 (3.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.232 (1.589, 6.576)
	Treatment P-value [b]		0.00063
	Interaction P-value [c]		0.98531

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	24 (9.3)	18 (7.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.280 (0.694, 2.359)
	Treatment P-value [b]		0.42826
	Interaction P-value [c]		0.63916
Ocular disorders	No. of Events (%)	80 (30.9)	21 (8.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.212 (2.604, 6.812)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.40870

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Peripheral Neuropathy	No. of Events (%)	134 (51.7)	92 (36.1)
	Median Survival Est. (95% CI)	5.91 (4.63, 8.61)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.402 (1.075, 1.829)
	Treatment P-value [b]		0.01199
	Interaction P-value [c]		0.65631
Skin reactions	No. of Events (%)	143 (55.2)	54 (21.2)
	Median Survival Est. (95% CI)	3.35 (1.45, 10.84)	NC (28.32, NC)
	Hazard Ratio (95% CI) [a]		3.377 (2.468, 4.622)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.11801

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Any	No. of Events (%)	27 (73.0)	22 (61.1)
	Median Survival Est. (95% CI)	0.82 (0.53, 3.06)	2.27 (0.56, NC)
	Hazard Ratio (95% CI) [a]		1.446 (0.823, 2.540)
	Treatment P-value [b]		0.22854
	Interaction P-value [c]		0.27235
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]		0.98531

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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]		1.970 (0.361, 10.758)
	Treatment P-value [b]		0.42839
	Interaction P-value [c]		0.63916
Ocular disorders	No. of Events (%)	7 (18.9)	3 (8.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.300 (0.595, 8.894)
	Treatment P-value [b]		0.21235
	Interaction P-value [c]		0.40870

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Peripheral Neuropathy	No. of Events (%)	19 (51.4)	12 (33.3)
	Median Survival Est. (95% CI)	4.83 (3.22, NC)	NC (4.44, NC)
	Hazard Ratio (95% CI) [a]		1.670 (0.811, 3.441)
	Treatment P-value [b]		0.18995
	Interaction P-value [c]		0.65631
Skin reactions	No. of Events (%)	20 (54.1)	13 (36.1)
	Median Survival Est. (95% CI)	2.79 (0.59, NC)	NC (3.71, NC)
	Hazard Ratio (95% CI) [a]		1.834 (0.912, 3.689)
	Treatment P-value [b]		0.10221
	Interaction P-value [c]		0.11801

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Any	No. of Events (%)	50 (82.0)	24 (49.0)
	Median Survival Est. (95% CI)	0.56 (0.36, 0.99)	6.51 (1.84, NC)
	Hazard Ratio (95% CI) [a]		2.742 (1.682, 4.469)
	Treatment P-value [b]		0.00003
	Interaction P-value [c]		0.16949
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]		6.659 (0.833, 53.248)
	Treatment P-value [b]		0.03712
	Interaction P-value [c]		0.38534

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)	5 (10.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.452 (0.487, 4.335)
	Treatment P-value [b]		0.46583
	Interaction P-value [c]		0.98939
Ocular disorders	No. of Events (%)	16 (26.2)	2 (4.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.770 (1.557, 29.443)
	Treatment P-value [b]		0.00314
	Interaction P-value [c]		0.51926

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Peripheral Neuropathy	No. of Events (%)	36 (59.0)	17 (34.7)
	Median Survival Est. (95% CI)	4.60 (2.99, 11.99)	NC (5.49, NC)
	Hazard Ratio (95% CI) [a]		1.747 (0.981, 3.112)
	Treatment P-value [b]		0.05949
	Interaction P-value [c]		0.48193
Skin reactions	No. of Events (%)	37 (60.7)	13 (26.5)
	Median Survival Est. (95% CI)	1.31 (0.49, 11.86)	NC (18.79, NC)
	Hazard Ratio (95% CI) [a]		3.343 (1.776, 6.295)
	Treatment P-value [b]		0.00009
	Interaction P-value [c]		0.89469

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Non-responder

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Any	No. of Events (%)	158 (78.2)	108 (53.5)
	Median Survival Est. (95% CI)	0.95 (0.69, 1.22)	2.79 (1.87, 9.03)
	Hazard Ratio (95% CI) [a]		1.871 (1.463, 2.393)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.16949
Hyperglycemia	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]		2.492 (1.147, 5.414)
	Treatment P-value [b]		0.01823
	Interaction P-value [c]		0.38534

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Non-responder

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Infusion related reaction	No. of Events (%)	18 (8.9)	12 (5.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.465 (0.706, 3.043)
	Treatment P-value [b]		0.30821
	Interaction P-value [c]		0.98939
Ocular disorders	No. of Events (%)	64 (31.7)	18 (8.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.053 (2.402, 6.839)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.51926

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Non-responder

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=202)	Chemotherapy (N=202)
Peripheral Neuropathy	No. of Events (%)	101 (50.0)	72 (35.6)
	Median Survival Est. (95% CI)	6.34 (4.63, 8.80)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.383 (1.022, 1.872)
	Treatment P-value [b]		0.03457
	Interaction P-value [c]		0.48193
Skin reactions	No. of Events (%)	115 (56.9)	47 (23.3)
	Median Survival Est. (95% CI)	2.56 (1.35, 7.49)	28.32 (28.32, NC)
	Hazard Ratio (95% CI) [a]		3.185 (2.267, 4.475)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.89469

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

3.10.2 Nicht schwer

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)
Any	No. of Events (%)	78 (73.6)	54 (52.4)
	Median Survival Est. (95% CI)	1.41 (0.82, 3.06)	3.78 (2.14, NC)
	Hazard Ratio (95% CI) [a]		1.681 (1.188, 2.378)
	Treatment P-value [b]		0.00337
	Interaction P-value [c]		0.27973
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]		4.737 (0.553, 40.550)
	Treatment P-value [b]		0.11638
	Interaction P-value [c]		0.57288

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	8 (7.5)	8 (7.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.923 (0.346, 2.461)
	Treatment P-value [b]		0.85406
	Interaction P-value [c]		0.51056
Ocular 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]		3.262 (1.400, 7.602)
	Treatment P-value [b]		0.00385
	Interaction P-value [c]		0.62948

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Peripheral Neuropathy	No. of Events (%)	53 (50.0)	36 (35.0)
	Median Survival Est. (95% CI)	6.93 (5.13, NC)	NC (9.07, NC)
	Hazard Ratio (95% CI) [a]		1.315 (0.861, 2.008)
	Treatment P-value [b]		0.20154
	Interaction P-value [c]		0.54052
Skin reactions	No. of Events (%)	55 (51.9)	23 (22.3)
	Median Survival Est. (95% CI)	8.08 (1.54, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.922 (1.795, 4.755)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.94313

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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=190)	Chemotherapy (N=188)
Any	No. of Events (%)	151 (79.5)	97 (51.6)
	Median Survival Est. (95% CI)	0.95 (0.72, 1.22)	3.94 (2.40, NC)
	Hazard Ratio (95% CI) [a]		2.132 (1.649, 2.756)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.27973
Hyperglycemia	No. of Events (%)	17 (8.9)	7 (3.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.430 (1.007, 5.864)
	Treatment P-value [b]		0.04357
	Interaction P-value [c]		0.57288

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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=190)	Chemotherapy (N=188)
Infusion related reaction	No. of Events (%)	17 (8.9)	12 (6.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.394 (0.666, 2.920)
	Treatment P-value [b]		0.36084
	Interaction P-value [c]		0.51056
Ocular disorders	No. of Events (%)	62 (32.6)	17 (9.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.175 (2.440, 7.141)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.62948

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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=190)	Chemotherapy (N=188)
Peripheral Neuropathy	No. of Events (%)	100 (52.6)	67 (35.6)
	Median Survival Est. (95% CI)	4.86 (4.04, 7.92)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.549 (1.136, 2.111)
	Treatment P-value [b]		0.00590
	Interaction P-value [c]		0.54052
Skin reactions	No. of Events (%)	102 (53.7)	43 (22.9)
	Median Survival Est. (95% CI)	2.79 (1.41, NC)	NC (28.32, NC)
	Hazard Ratio (95% CI) [a]		2.987 (2.090, 4.268)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.94313

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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=245)	Chemotherapy (N=226)
Any	No. of Events (%)	189 (77.1)	116 (51.3)
	Median Survival Est. (95% CI)	0.99 (0.82, 1.41)	3.94 (2.40, 12.29)
	Hazard Ratio (95% CI) [a]		1.970 (1.561, 2.485)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.86322
Hyperglycemia	No. of Events (%)	15 (6.1)	5 (2.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.699 (0.981, 7.431)
	Treatment P-value [b]		0.04411
	Interaction P-value [c]		0.82458

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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=245)	Chemotherapy (N=226)
Infusion related reaction	No. of Events (%)	25 (10.2)	12 (5.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.892 (0.950, 3.767)
	Treatment P-value [b]		0.06383
	Interaction P-value [c]		0.98628
Ocular disorders	No. of Events (%)	66 (26.9)	16 (7.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.092 (2.370, 7.066)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.88670

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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=245)	Chemotherapy (N=226)
Peripheral Neuropathy	No. of Events (%)	130 (53.1)	81 (35.8)
	Median Survival Est. (95% CI)	5.32 (4.60, 8.31)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.459 (1.105, 1.926)
	Treatment P-value [b]		0.00653
	Interaction P-value [c]		0.86352
Skin reactions	No. of Events (%)	132 (53.9)	51 (22.6)
	Median Survival Est. (95% CI)	4.11 (1.68, 11.86)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.056 (2.211, 4.225)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.61511

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Any	No. of Events (%)	40 (78.4)	35 (53.8)
	Median Survival Est. (95% CI)	1.18 (0.56, 1.91)	3.29 (1.22, NC)
	Hazard Ratio (95% CI) [a]		1.883 (1.196, 2.967)
	Treatment P-value [b]		0.00739
	Interaction P-value [c]		0.86322
Hyperglycemia	No. of Events (%)	7 (13.7)	3 (4.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.268 (0.845, 12.641)
	Treatment P-value [b]		0.07513
	Interaction P-value [c]		0.82458

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Infusion related reaction	No. of Events (%)	0	8 (12.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.01010
	Interaction P-value [c]		0.98628
Ocular 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]		3.808 (1.666, 8.703)
	Treatment P-value [b]		0.00099
	Interaction P-value [c]		0.88670

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Peripheral 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]		1.379 (0.768, 2.474)
	Treatment P-value [b]		0.30684
	Interaction P-value [c]		0.86352
Skin reactions	No. of Events (%)	25 (49.0)	15 (23.1)
	Median Survival Est. (95% CI)	3.68 (1.25, NC)	28.32 (23.52, NC)
	Hazard Ratio (95% CI) [a]		2.542 (1.339, 4.826)
	Treatment P-value [b]		0.00348
	Interaction P-value [c]		0.61511

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Any	No. of Events (%)	187 (79.9)	109 (49.8)
	Median Survival Est. (95% CI)	0.99 (0.82, 1.35)	4.47 (2.76, NC)
	Hazard Ratio (95% CI) [a]		2.182 (1.721, 2.767)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.05162
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]		4.612 (1.575, 13.503)
	Treatment P-value [b]		0.00170
	Interaction P-value [c]		0.04703

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	18 (7.7)	15 (6.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.074 (0.541, 2.133)
	Treatment P-value [b]		0.85326
	Interaction P-value [c]		0.49305
Ocular disorders	No. of Events (%)	70 (29.9)	17 (7.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.208 (2.477, 7.150)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.45624

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Peripheral Neuropathy	No. of Events (%)	126 (53.8)	74 (33.8)
	Median Survival Est. (95% CI)	5.29 (4.21, 8.31)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.628 (1.222, 2.169)
	Treatment P-value [b]		0.00072
	Interaction P-value [c]		0.10930
Skin reactions	No. of Events (%)	124 (53.0)	45 (20.5)
	Median Survival Est. (95% CI)	4.21 (1.68, 14.55)	NC (28.32, NC)
	Hazard Ratio (95% CI) [a]		3.256 (2.314, 4.582)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.32045

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Any	No. of Events (%)	42 (67.7)	42 (58.3)
	Median Survival Est. (95% CI)	1.28 (0.66, 2.33)	3.38 (0.82, 9.03)
	Hazard Ratio (95% CI) [a]		1.343 (0.875, 2.061)
	Treatment P-value [b]		0.21405
	Interaction P-value [c]		0.05162
Hyperglycemia	No. of Events (%)	2 (3.2)	4 (5.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.602 (0.110, 3.288)
	Treatment P-value [b]		0.59307
	Interaction P-value [c]		0.04703

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)	5 (6.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.714 (0.544, 5.403)
	Treatment P-value [b]		0.36212
	Interaction P-value [c]		0.49305
Ocular disorders	No. of Events (%)	15 (24.2)	7 (9.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.832 (1.154, 6.946)
	Treatment P-value [b]		0.01444
	Interaction P-value [c]		0.45624

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Peripheral Neuropathy	No. of Events (%)	27 (43.5)	29 (40.3)
	Median Survival Est. (95% CI)	6.93 (4.63, NC)	NC (5.26, NC)
	Hazard Ratio (95% CI) [a]		0.999 (0.591, 1.688)
	Treatment P-value [b]		0.99126
	Interaction P-value [c]		0.10930
Skin reactions	No. of Events (%)	33 (53.2)	21 (29.2)
	Median Survival Est. (95% CI)	2.73 (0.92, NC)	NC (17.68, NC)
	Hazard Ratio (95% CI) [a]		2.347 (1.357, 4.060)
	Treatment P-value [b]		0.00117
	Interaction P-value [c]		0.32045

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Any	No. of Events (%)	89 (73.0)	52 (42.3)
	Median Survival Est. (95% CI)	1.38 (0.95, 2.07)	NC (5.49, NC)
	Hazard Ratio (95% CI) [a]		2.175 (1.542, 3.066)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.55699
Hyperglycemia	No. of Events (%)	11 (9.0)	5 (4.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.139 (0.743, 6.160)
	Treatment P-value [b]		0.14826
	Interaction P-value [c]		0.95560

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

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	6 (4.9)	8 (6.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.706 (0.245, 2.035)
	Treatment P-value [b]		0.52137
	Interaction P-value [c]		0.26676
Ocular disorders	No. of Events (%)	50 (41.0)	6 (4.9)
	Median Survival Est. (95% CI)	NC (6.05, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		10.270 (4.401, 23.966)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.00230

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Peripheral Neuropathy	No. of Events (%)	64 (52.5)	32 (26.0)
	Median Survival Est. (95% CI)	5.78 (3.29, 8.80)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.269 (1.484, 3.470)
	Treatment P-value [b]		0.00011
	Interaction P-value [c]		0.02226
Skin reactions	No. of Events (%)	56 (45.9)	19 (15.4)
	Median Survival Est. (95% CI)	12.68 (3.78, NC)	NC (28.32, NC)
	Hazard Ratio (95% CI) [a]		3.427 (2.036, 5.767)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.82963

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Any	No. of Events (%)	35 (83.3)	22 (56.4)
	Median Survival Est. (95% CI)	0.95 (0.53, 1.51)	3.78 (2.27, NC)
	Hazard Ratio (95% CI) [a]		2.206 (1.293, 3.763)
	Treatment P-value [b]		0.00146
	Interaction P-value [c]		0.55699
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]		0.95560

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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]		4.992 (0.583, 42.731)
	Treatment P-value [b]		0.10269
	Interaction P-value [c]		0.26676
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]		1.209 (0.501, 2.919)
	Treatment P-value [b]		0.64397
	Interaction P-value [c]		0.00230

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Peripheral 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]		1.378 (0.728, 2.608)
	Treatment P-value [b]		0.32225
	Interaction P-value [c]		0.02226
Skin reactions	No. of Events (%)	24 (57.1)	10 (25.6)
	Median Survival Est. (95% CI)	2.33 (0.59, NC)	NC (8.97, NC)
	Hazard Ratio (95% CI) [a]		2.948 (1.409, 6.168)
	Treatment P-value [b]		0.00177
	Interaction P-value [c]		0.82963

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Any	No. of Events (%)	105 (79.5)	77 (59.7)
	Median Survival Est. (95% CI)	0.92 (0.53, 1.35)	2.30 (1.48, 3.48)
	Hazard Ratio (95% CI) [a]		1.740 (1.296, 2.336)
	Treatment P-value [b]		0.00025
	Interaction P-value [c]		0.55699
Hyperglycemia	No. of Events (%)	5 (3.8)	3 (2.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.628 (0.389, 6.815)
	Treatment P-value [b]		0.53198
	Interaction P-value [c]		0.95560

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)	11 (8.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.234 (0.560, 2.721)
	Treatment P-value [b]		0.59991
	Interaction P-value [c]		0.26676
Ocular disorders	No. of Events (%)	24 (18.2)	9 (7.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.692 (1.251, 5.792)
	Treatment P-value [b]		0.00922
	Interaction P-value [c]		0.00230

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Peripheral Neuropathy	No. of Events (%)	66 (50.0)	55 (42.6)
	Median Survival Est. (95% CI)	6.34 (4.83, NC)	NC (3.94, NC)
	Hazard Ratio (95% CI) [a]		1.039 (0.726, 1.486)
	Treatment P-value [b]		0.83459
	Interaction P-value [c]		0.02226
Skin reactions	No. of Events (%)	77 (58.3)	37 (28.7)
	Median Survival Est. (95% CI)	1.41 (0.72, 7.49)	NC (23.52, NC)
	Hazard Ratio (95% CI) [a]		2.799 (1.890, 4.145)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.82963

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Any	No. of Events (%)	100 (83.3)	70 (58.8)
	Median Survival Est. (95% CI)	0.72 (0.49, 0.95)	2.40 (1.68, 6.51)
	Hazard Ratio (95% CI) [a]		2.117 (1.558, 2.878)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.56129
Hyperglycemia	No. of Events (%)	8 (6.7)	4 (3.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.023 (0.609, 6.718)
	Treatment P-value [b]		0.23994
	Interaction P-value [c]		0.54419

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)	9 (7.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.683 (0.736, 3.846)
	Treatment P-value [b]		0.21672
	Interaction P-value [c]		0.25684
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]		4.833 (2.237, 10.439)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.44352

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Peripheral Neuropathy	No. of Events (%)	70 (58.3)	48 (40.3)
	Median Survival Est. (95% CI)	5.06 (3.71, 8.80)	NC (9.07, NC)
	Hazard Ratio (95% CI) [a]		1.509 (1.045, 2.180)
	Treatment P-value [b]		0.02862
	Interaction P-value [c]		0.81395
Skin reactions	No. of Events (%)	75 (62.5)	32 (26.9)
	Median Survival Est. (95% CI)	1.41 (0.53, 7.06)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.437 (2.269, 5.205)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.41097

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Any	No. of Events (%)	129 (73.3)	81 (47.1)
	Median Survival Est. (95% CI)	1.35 (0.99, 2.07)	5.82 (2.79, NC)
	Hazard Ratio (95% CI) [a]		1.873 (1.418, 2.475)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.56129
Hyperglycemia	No. of Events (%)	14 (8.0)	4 (2.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.356 (1.104, 10.202)
	Treatment P-value [b]		0.02318
	Interaction P-value [c]		0.54419

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	10 (5.7)	11 (6.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.845 (0.359, 1.991)
	Treatment P-value [b]		0.69847
	Interaction P-value [c]		0.25684
Ocular disorders	No. of Events (%)	51 (29.0)	16 (9.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.329 (1.898, 5.839)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.44352

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Peripheral Neuropathy	No. of Events (%)	83 (47.2)	55 (32.0)
	Median Survival Est. (95% CI)	6.93 (4.60, 10.84)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.421 (1.011, 1.998)
	Treatment P-value [b]		0.04162
	Interaction P-value [c]		0.81395
Skin reactions	No. of Events (%)	82 (46.6)	34 (19.8)
	Median Survival Est. (95% CI)	14.55 (2.56, NC)	28.32 (23.52, NC)
	Hazard Ratio (95% CI) [a]		2.699 (1.808, 4.027)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.41097

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Any	No. of Events (%)	66 (71.7)	40 (46.0)
	Median Survival Est. (95% CI)	0.95 (0.59, 1.91)	5.49 (2.76, NC)
	Hazard Ratio (95% CI) [a]		2.173 (1.466, 3.222)
	Treatment P-value [b]		0.00009
	Interaction P-value [c]		0.52375
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]		5.686 (0.684, 47.249)
	Treatment P-value [b]		0.06457
	Interaction P-value [c]		0.43438

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)	3 (3.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.566 (0.374, 6.554)
	Treatment P-value [b]		0.54686
	Interaction P-value [c]		0.69563
Ocular disorders	No. of Events (%)	23 (25.0)	8 (9.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.931 (1.311, 6.554)
	Treatment P-value [b]		0.00650
	Interaction P-value [c]		0.43826

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Peripheral 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]		1.240 (0.772, 1.991)
	Treatment P-value [b]		0.36671
	Interaction P-value [c]		0.43022
Skin reactions	No. of Events (%)	50 (54.3)	16 (18.4)
	Median Survival Est. (95% CI)	2.17 (0.95, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.788 (2.156, 6.656)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.30909

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Any	No. of Events (%)	163 (79.9)	111 (54.4)
	Median Survival Est. (95% CI)	1.05 (0.82, 1.45)	3.45 (2.14, 9.03)
	Hazard Ratio (95% CI) [a]		1.871 (1.468, 2.384)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.52375
Hyperglycemia	No. of Events (%)	16 (7.8)	7 (3.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.276 (0.936, 5.533)
	Treatment P-value [b]		0.06317
	Interaction P-value [c]		0.43438

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	20 (9.8)	17 (8.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.144 (0.599, 2.185)
	Treatment P-value [b]		0.67282
	Interaction P-value [c]		0.69563
Ocular disorders	No. of Events (%)	62 (30.4)	16 (7.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.309 (2.487, 7.466)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.43826

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Peripheral Neuropathy	No. of Events (%)	113 (55.4)	73 (35.8)
	Median Survival Est. (95% CI)	5.68 (4.60, 8.34)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.552 (1.156, 2.084)
	Treatment P-value [b]		0.00291
	Interaction P-value [c]		0.43022
Skin reactions	No. of Events (%)	107 (52.5)	50 (24.5)
	Median Survival Est. (95% CI)	7.95 (1.71, NC)	NC (28.32, NC)
	Hazard Ratio (95% CI) [a]		2.696 (1.926, 3.773)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.30909

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Any	No. of Events (%)	107 (76.4)	67 (62.6)
	Median Survival Est. (95% CI)	1.15 (0.76, 1.71)	1.48 (0.82, 2.79)
	Hazard Ratio (95% CI) [a]		1.304 (0.961, 1.771)
	Treatment P-value [b]		0.09093
	Interaction P-value [c]		0.00473
Hyperglycemia	No. of Events (%)	6 (4.3)	3 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.495 (0.374, 5.979)
	Treatment P-value [b]		0.58257
	Interaction P-value [c]		0.18087

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Infusion related reaction	No. of Events (%)	11 (7.9)	7 (6.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.166 (0.452, 3.008)
	Treatment P-value [b]		0.76142
	Interaction P-value [c]		0.47122
Ocular disorders	No. of Events (%)	33 (23.6)	7 (6.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.875 (1.714, 8.761)
	Treatment P-value [b]		0.00042
	Interaction P-value [c]		0.01276

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Peripheral Neuropathy	No. of Events (%)	75 (53.6)	59 (55.1)
	Median Survival Est. (95% CI)	5.29 (4.21, 7.62)	3.68 (1.54, 9.07)
	Hazard Ratio (95% CI) [a]		0.725 (0.515, 1.020)
	Treatment P-value [b]		0.07139
	Interaction P-value [c]		<.00001
Skin reactions	No. of Events (%)	73 (52.1)	27 (25.2)
	Median Survival Est. (95% CI)	7.06 (1.45, NC)	NC (28.32, NC)
	Hazard Ratio (95% CI) [a]		2.561 (1.647, 3.984)
	Treatment P-value [b]		0.00002
	Interaction P-value [c]		0.52536

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Docetaxel

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Any	No. of Events (%)	68 (80.0)	56 (51.4)
	Median Survival Est. (95% CI)	0.92 (0.49, 1.41)	4.60 (2.43, NC)
	Hazard Ratio (95% CI) [a]		2.306 (1.617, 3.287)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.00473
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]		13.052 (1.671, 101.984)
	Treatment P-value [b]		0.00134
	Interaction P-value [c]		0.18087

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: 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]		1.834 (0.698, 4.822)
	Treatment P-value [b]		0.18296
	Interaction P-value [c]		0.47122
Ocular disorders	No. of Events (%)	21 (24.7)	14 (12.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.929 (0.981, 3.794)
	Treatment P-value [b]		0.05435
	Interaction P-value [c]		0.01276

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Docetaxel

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=85)	Chemotherapy (N=109)
Peripheral Neuropathy	No. of Events (%)	42 (49.4)	30 (27.5)
	Median Survival Est. (95% CI)	8.31 (4.21, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.863 (1.166, 2.977)
	Treatment P-value [b]		0.00793
	Interaction P-value [c]		<.00001
Skin reactions	No. of Events (%)	49 (57.6)	28 (25.7)
	Median Survival Est. (95% CI)	1.54 (0.72, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.070 (1.929, 4.888)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.52536

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Vinflunine

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Any	No. of Events (%)	54 (76.1)	28 (37.3)
	Median Survival Est. (95% CI)	1.15 (0.85, 1.87)	NC (6.51, NC)
	Hazard Ratio (95% CI) [a]		2.990 (1.890, 4.730)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.00473
Hyperglycemia	No. of Events (%)	6 (8.5)	4 (5.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.603 (0.452, 5.681)
	Treatment P-value [b]		0.46409
	Interaction P-value [c]		0.18087

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Vinflunine

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Infusion related reaction	No. of Events (%)	4 (5.6)	6 (8.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.682 (0.192, 2.417)
	Treatment P-value [b]		0.53076
	Interaction P-value [c]		0.47122
Ocular disorders	No. of Events (%)	31 (43.7)	3 (4.0)
	Median Survival Est. (95% CI)	9.95 (3.29, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		14.834 (4.532, 48.551)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.01276

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Vinflunine

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Peripheral Neuropathy	No. of Events (%)	36 (50.7)	14 (18.7)
	Median Survival Est. (95% CI)	5.78 (2.89, 10.84)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.552 (1.915, 6.589)
	Treatment P-value [b]		0.00002
	Interaction P-value [c]		<.00001
Skin reactions	No. of Events (%)	35 (49.3)	11 (14.7)
	Median Survival Est. (95% CI)	8.08 (2.17, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.076 (2.069, 8.028)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.52536

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Any	No. of Events (%)	80 (83.3)	54 (52.9)
	Median Survival Est. (95% CI)	0.95 (0.59, 1.41)	3.48 (1.58, NC)
	Hazard Ratio (95% CI) [a]		2.111 (1.493, 2.985)
	Treatment P-value [b]		0.00002
	Interaction P-value [c]		0.60414
Hyperglycemia	No. of Events (%)	9 (9.4)	6 (5.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.606 (0.572, 4.513)
	Treatment P-value [b]		0.38765
	Interaction P-value [c]		0.14848

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)	6 (5.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.042 (0.336, 3.232)
	Treatment P-value [b]		0.95129
	Interaction P-value [c]		0.78735
Ocular disorders	No. of Events (%)	24 (25.0)	7 (6.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.875 (1.669, 8.992)
	Treatment P-value [b]		0.00073
	Interaction P-value [c]		0.97447

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Peripheral Neuropathy	No. of Events (%)	52 (54.2)	37 (36.3)
	Median Survival Est. (95% CI)	5.13 (3.75, 8.31)	NC (7.43, NC)
	Hazard Ratio (95% CI) [a]		1.490 (0.977, 2.271)
	Treatment P-value [b]		0.06461
	Interaction P-value [c]		0.90852
Skin reactions	No. of Events (%)	57 (59.4)	24 (23.5)
	Median Survival Est. (95% CI)	1.68 (0.92, 7.95)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.347 (2.076, 5.396)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.55384

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Any	No. of Events (%)	149 (74.5)	97 (51.3)
	Median Survival Est. (95% CI)	1.15 (0.85, 1.61)	4.47 (2.37, NC)
	Hazard Ratio (95% CI) [a]		1.884 (1.458, 2.435)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.60414
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]		6.108 (1.378, 27.075)
	Treatment P-value [b]		0.00554
	Interaction P-value [c]		0.14848

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	19 (9.5)	14 (7.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.251 (0.627, 2.496)
	Treatment P-value [b]		0.51699
	Interaction P-value [c]		0.78735
Ocular disorders	No. of Events (%)	61 (30.5)	17 (9.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.812 (2.227, 6.526)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.97447

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Peripheral Neuropathy	No. of Events (%)	101 (50.5)	66 (34.9)
	Median Survival Est. (95% CI)	6.60 (4.40, 10.84)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.445 (1.059, 1.970)
	Treatment P-value [b]		0.01869
	Interaction P-value [c]		0.90852
Skin reactions	No. of Events (%)	100 (50.0)	42 (22.2)
	Median Survival Est. (95% CI)	8.08 (2.33, NC)	28.32 (28.32, NC)
	Hazard Ratio (95% CI) [a]		2.793 (1.947, 4.007)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.55384

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Any	No. of Events (%)	202 (78.0)	130 (51.0)
	Median Survival Est. (95% CI)	1.05 (0.92, 1.41)	4.47 (2.76, NC)
	Hazard Ratio (95% CI) [a]		2.007 (1.608, 2.505)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.47876
Hyperglycemia	No. of Events (%)	20 (7.7)	8 (3.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.461 (1.083, 5.589)
	Treatment P-value [b]		0.02654
	Interaction P-value [c]		0.98762

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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 (%)	22 (8.5)	18 (7.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.171 (0.628, 2.185)
	Treatment P-value [b]		0.62417
	Interaction P-value [c]		0.81078
Ocular disorders	No. of Events (%)	78 (30.1)	21 (8.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.093 (2.527, 6.628)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.43181

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Peripheral Neuropathy	No. of Events (%)	134 (51.7)	91 (35.7)
	Median Survival Est. (95% CI)	5.91 (4.63, 8.61)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.430 (1.096, 1.867)
	Treatment P-value [b]		0.00807
	Interaction P-value [c]		0.68987
Skin reactions	No. of Events (%)	138 (53.3)	54 (21.2)
	Median Survival Est. (95% CI)	4.11 (1.91, 14.55)	NC (28.32, NC)
	Hazard Ratio (95% CI) [a]		3.193 (2.330, 4.377)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.20865

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: >=3 lines

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Any	No. of Events (%)	27 (73.0)	21 (58.3)
	Median Survival Est. (95% CI)	0.82 (0.53, 3.06)	2.40 (0.59, NC)
	Hazard Ratio (95% CI) [a]		1.609 (0.909, 2.848)
	Treatment P-value [b]		0.13201
	Interaction P-value [c]		0.47876
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]		0.98762

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: >=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]		1.476 (0.247, 8.832)
	Treatment P-value [b]		0.64963
	Interaction P-value [c]		0.81078
Ocular disorders	No. of Events (%)	7 (18.9)	3 (8.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.301 (0.595, 8.898)
	Treatment P-value [b]		0.21235
	Interaction P-value [c]		0.43181

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: >=3 lines

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Peripheral Neuropathy	No. of Events (%)	19 (51.4)	12 (33.3)
	Median Survival Est. (95% CI)	4.83 (3.22, NC)	NC (4.44, NC)
	Hazard Ratio (95% CI) [a]		1.673 (0.812, 3.446)
	Treatment P-value [b]		0.18995
	Interaction P-value [c]		0.68987
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]		1.925 (0.934, 3.969)
	Treatment P-value [b]		0.09191
	Interaction P-value [c]		0.20865

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Any	No. of Events (%)	50 (82.0)	24 (49.0)
	Median Survival Est. (95% CI)	0.82 (0.46, 1.28)	6.51 (1.84, NC)
	Hazard Ratio (95% CI) [a]		2.677 (1.642, 4.363)
	Treatment P-value [b]		0.00005
	Interaction P-value [c]		0.22706
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]		0.98975

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)	5 (10.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.275 (0.417, 3.898)
	Treatment P-value [b]		0.62626
	Interaction P-value [c]		0.97361
Ocular disorders	No. of Events (%)	16 (26.2)	2 (4.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.770 (1.557, 29.445)
	Treatment P-value [b]		0.00314
	Interaction P-value [c]		0.49043

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Peripheral Neuropathy	No. of Events (%)	36 (59.0)	17 (34.7)
	Median Survival Est. (95% CI)	4.60 (2.99, 11.99)	NC (5.49, NC)
	Hazard Ratio (95% CI) [a]		1.747 (0.981, 3.112)
	Treatment P-value [b]		0.05949
	Interaction P-value [c]		0.53090
Skin reactions	No. of Events (%)	36 (59.0)	13 (26.5)
	Median Survival Est. (95% CI)	1.41 (0.72, NC)	NC (18.79, NC)
	Hazard Ratio (95% CI) [a]		3.125 (1.656, 5.897)
	Treatment P-value [b]		0.00021
	Interaction P-value [c]		0.97193

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Any	No. of Events (%)	156 (77.2)	105 (52.0)
	Median Survival Est. (95% CI)	1.02 (0.76, 1.38)	3.45 (2.10, NC)
	Hazard Ratio (95% CI) [a]		1.911 (1.491, 2.451)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.22706
Hyperglycemia	No. of Events (%)	14 (6.9)	8 (4.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.739 (0.729, 4.147)
	Treatment P-value [b]		0.21330
	Interaction P-value [c]		0.98975

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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 (%)	16 (7.9)	12 (5.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.304 (0.617, 2.757)
	Treatment P-value [b]		0.49404
	Interaction P-value [c]		0.97361
Ocular disorders	No. of Events (%)	62 (30.7)	18 (8.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.909 (2.313, 6.608)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.49043

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Peripheral Neuropathy	No. of Events (%)	101 (50.0)	71 (35.1)
	Median Survival Est. (95% CI)	6.34 (4.63, 8.80)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.419 (1.047, 1.922)
	Treatment P-value [b]		0.02321
	Interaction P-value [c]		0.53090
Skin reactions	No. of Events (%)	110 (54.5)	46 (22.8)
	Median Survival Est. (95% CI)	3.68 (1.45, 12.68)	28.32 (28.32, NC)
	Hazard Ratio (95% CI) [a]		3.085 (2.185, 4.355)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.97193

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

3.10.3 Schwer

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)
Any	No. of Events (%)	20 (18.9)	4 (3.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.032 (1.720, 14.724)
	Treatment P-value [b]		0.00110
	Interaction P-value [c]		0.65782
Hyperglycemia	No. of Events (%)	3 (2.8)	2 (1.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.428 (0.239, 8.548)
	Treatment P-value [b]		0.71015
	Interaction P-value [c]		0.11516

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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=106)	Chemotherapy (N=103)
Peripheral 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]		6.761 (0.846, 54.053)
	Treatment P-value [b]		0.04356
	Interaction P-value [c]		0.20073
Skin reactions	No. of Events (%)	12 (11.3)	1 (1.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		11.914 (1.551, 91.519)
	Treatment P-value [b]		0.00246
	Interaction P-value [c]		0.61487

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Any	No. of Events (%)	59 (31.1)	17 (9.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.836 (2.236, 6.580)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.65782
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]		9.145 (2.121, 39.424)
	Treatment P-value [b]		0.00028
	Interaction P-value [c]		0.11516

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Peripheral Neuropathy	No. of Events (%)	16 (8.4)	9 (4.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.573 (0.695, 3.562)
	Treatment P-value [b]		0.27431
	Interaction P-value [c]		0.20073
Skin reactions	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]		6.693 (2.607, 17.183)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.61487

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Any	No. of Events (%)	62 (25.3)	14 (6.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.369 (2.446, 7.804)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.70397
Hyperglycemia	No. of Events (%)	15 (6.1)	3 (1.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.617 (1.336, 15.951)
	Treatment P-value [b]		0.00805
	Interaction P-value [c]		0.66374

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Peripheral Neuropathy	No. of Events (%)	19 (7.8)	6 (2.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.528 (1.009, 6.332)
	Treatment P-value [b]		0.04392
	Interaction P-value [c]		0.55424
Skin reactions	No. of Events (%)	36 (14.7)	4 (1.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		8.563 (3.048, 24.061)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.64863

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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=51)	Chemotherapy (N=65)
Any	No. of Events (%)	17 (33.3)	7 (10.8)
	Median Survival Est. (95% CI)	NC (6.70, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.562 (1.477, 8.591)
	Treatment P-value [b]		0.00228
	Interaction P-value [c]		0.70397
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]		7.956 (0.958, 66.106)
	Treatment P-value [b]		0.02332
	Interaction P-value [c]		0.66374

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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=51)	Chemotherapy (N=65)
Peripheral 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]		1.558 (0.418, 5.805)
	Treatment P-value [b]		0.44802
	Interaction P-value [c]		0.55424
Skin reactions	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]		5.554 (1.179, 26.164)
	Treatment P-value [b]		0.02081
	Interaction P-value [c]		0.64863

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Any	No. of Events (%)	69 (29.5)	15 (6.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.620 (2.643, 8.077)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.19624
Hyperglycemia	No. of Events (%)	19 (8.1)	4 (1.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.440 (1.510, 13.058)
	Treatment P-value [b]		0.00304
	Interaction P-value [c]		0.99085

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Peripheral Neuropathy	No. of Events (%)	23 (9.8)	8 (3.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.245 (1.003, 5.024)
	Treatment P-value [b]		0.04522
	Interaction P-value [c]		0.31806
Skin reactions	No. of Events (%)	37 (15.8)	2 (0.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		17.946 (4.324, 74.475)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.02751

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Any	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]		2.155 (0.783, 5.932)
	Treatment P-value [b]		0.10922
	Interaction P-value [c]		0.19624
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]		0.99085

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Peripheral Neuropathy	No. of Events (%)	1 (1.6)	2 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.618 (0.056, 6.817)
	Treatment P-value [b]		0.64388
	Interaction P-value [c]		0.31806
Skin reactions	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]		2.165 (0.634, 7.399)
	Treatment P-value [b]		0.15526
	Interaction P-value [c]		0.02751

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Any	No. of Events (%)	36 (29.5)	6 (4.9)
	Median Survival Est. (95% CI)	NC (20.70, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.556 (2.762, 15.563)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.02358
Hyperglycemia	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]		4.958 (1.086, 22.629)
	Treatment P-value [b]		0.02247
	Interaction P-value [c]		0.89938

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Peripheral Neuropathy	No. of Events (%)	16 (13.1)	3 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.052 (1.472, 17.342)
	Treatment P-value [b]		0.00442
	Interaction P-value [c]		0.05993
Skin reactions	No. of Events (%)	15 (12.3)	1 (0.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		15.110 (1.996, 114.399)
	Treatment P-value [b]		0.00043
	Interaction P-value [c]		0.44392

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Any	No. of Events (%)	15 (35.7)	1 (2.6)
	Median Survival Est. (95% CI)	NC (4.99, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		18.410 (2.433, 139.306)
	Treatment P-value [b]		0.00018
	Interaction P-value [c]		0.02358
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]		0.89938

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Peripheral 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]		0.05993
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]		0.44392

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Any	No. of Events (%)	28 (21.2)	14 (10.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.004 (1.055, 3.808)
	Treatment P-value [b]		0.03611
	Interaction P-value [c]		0.02358
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]		2.953 (0.596, 14.636)
	Treatment P-value [b]		0.15627
	Interaction P-value [c]		0.89938

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Peripheral Neuropathy	No. of Events (%)	6 (4.5)	7 (5.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		0.688 (0.231, 2.050)
	Treatment P-value [b]		0.48855
	Interaction P-value [c]		0.05993
Skin reactions	No. of Events (%)	17 (12.9)	5 (3.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.484 (1.285, 9.446)
	Treatment P-value [b]		0.01062
	Interaction P-value [c]		0.44392

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Any	No. of Events (%)	37 (30.8)	12 (10.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.645 (1.900, 6.993)
	Treatment P-value [b]		0.00004
	Interaction P-value [c]		0.63539
Hyperglycemia	No. of Events (%)	8 (6.7)	1 (0.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		8.175 (1.022, 65.360)
	Treatment P-value [b]		0.01851
	Interaction P-value [c]		0.59139

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Peripheral Neuropathy	No. of Events (%)	8 (6.7)	6 (5.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.261 (0.437, 3.634)
	Treatment P-value [b]		0.65505
	Interaction P-value [c]		0.22816
Skin reactions	No. of Events (%)	24 (20.0)	4 (3.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.639 (2.303, 19.137)
	Treatment P-value [b]		0.00007
	Interaction P-value [c]		0.67642

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Any	No. of Events (%)	42 (23.9)	9 (5.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.611 (2.244, 9.472)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.63539
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]		4.203 (1.197, 14.757)
	Treatment P-value [b]		0.01380
	Interaction P-value [c]		0.59139

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Peripheral Neuropathy	No. of Events (%)	16 (9.1)	4 (2.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.217 (1.075, 9.629)
	Treatment P-value [b]		0.02890
	Interaction P-value [c]		0.22816
Skin reactions	No. of Events (%)	20 (11.4)	2 (1.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.736 (2.275, 41.662)
	Treatment P-value [b]		0.00019
	Interaction P-value [c]		0.67642

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Any	No. of Events (%)	25 (27.2)	7 (8.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.532 (1.527, 8.170)
	Treatment P-value [b]		0.00173
	Interaction P-value [c]		0.72661
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]		0.98930

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Peripheral Neuropathy	No. of Events (%)	6 (6.5)	4 (4.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.070 (0.301, 3.801)
	Treatment P-value [b]		0.88518
	Interaction P-value [c]		0.23291
Skin reactions	No. of Events (%)	15 (16.3)	2 (2.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.419 (1.696, 32.452)
	Treatment P-value [b]		0.00204
	Interaction P-value [c]		0.98446

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Any	No. of Events (%)	54 (26.5)	14 (6.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.240 (2.355, 7.632)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.72661
Hyperglycemia	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]		3.764 (1.249, 11.342)
	Treatment P-value [b]		0.01145
	Interaction P-value [c]		0.98930

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Peripheral Neuropathy	No. of Events (%)	18 (8.8)	6 (2.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.780 (1.103, 7.004)
	Treatment P-value [b]		0.02278
	Interaction P-value [c]		0.23291
Skin reactions	No. of Events (%)	29 (14.2)	4 (2.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.553 (2.655, 21.487)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.98446

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Paclitaxel

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Any	No. of Events (%)	41 (29.3)	14 (13.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.423 (1.320, 4.445)
	Treatment P-value [b]		0.00371
	Interaction P-value [c]		0.12912
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]		7.701 (0.986, 60.160)
	Treatment P-value [b]		0.02104
	Interaction P-value [c]		0.76991

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Paclitaxel

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=140)	Chemotherapy (N=107)
Peripheral Neuropathy	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]		0.919 (0.408, 2.070)
	Treatment P-value [b]		0.80852
	Interaction P-value [c]		0.99989
Skin reactions	No. of Events (%)	24 (17.1)	3 (2.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.439 (1.939, 21.387)
	Treatment P-value [b]		0.00047
	Interaction P-value [c]		0.95113

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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 (%)	19 (22.4)	4 (3.7)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.435 (2.189, 18.920)
	Treatment P-value [b]		0.00011
	Interaction P-value [c]		0.12912
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]		6.470 (0.756, 55.394)
	Treatment P-value [b]		0.04640
	Interaction P-value [c]		0.76991

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Peripheral Neuropathy	No. of Events (%)	3 (3.5)	0
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		NA (NA , NA)
	Treatment P-value [b]		0.09116
	Interaction P-value [c]		0.99989
Skin reactions	No. of Events (%)	13 (15.3)	2 (1.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		8.760 (1.976, 38.829)
	Treatment P-value [b]		0.00067
	Interaction P-value [c]		0.95113

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Vinflunine

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Any	No. of Events (%)	19 (26.8)	3 (4.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.410 (2.192, 25.044)
	Treatment P-value [b]		0.00012
	Interaction P-value [c]		0.12912
Hyperglycemia	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]		3.199 (0.646, 15.851)
	Treatment P-value [b]		0.13708
	Interaction P-value [c]		0.76991

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Vinflunine

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=71)	Chemotherapy (N=75)
Peripheral Neuropathy	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]		0.00683
	Interaction P-value [c]		0.99989
Skin reactions	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]		7.496 (0.922, 60.923)
	Treatment P-value [b]		0.02561
	Interaction P-value [c]		0.95113

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Any	No. of Events (%)	25 (26.0)	12 (11.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.375 (1.193, 4.727)
	Treatment P-value [b]		0.01339
	Interaction P-value [c]		0.05681
Hyperglycemia	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]		2.111 (0.528, 8.443)
	Treatment P-value [b]		0.29232
	Interaction P-value [c]		0.12489

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Peripheral Neuropathy	No. of Events (%)	7 (7.3)	5 (4.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.360 (0.431, 4.285)
	Treatment P-value [b]		0.59607
	Interaction P-value [c]		0.35446
Skin reactions	No. of Events (%)	17 (17.7)	4 (3.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.857 (1.634, 14.437)
	Treatment P-value [b]		0.00193
	Interaction P-value [c]		0.27969

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Any	No. of Events (%)	54 (27.0)	9 (4.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.190 (3.056, 12.537)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.05681
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]		14.402 (1.904, 108.930)
	Treatment P-value [b]		0.00057
	Interaction P-value [c]		0.12489

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Peripheral Neuropathy	No. of Events (%)	17 (8.5)	5 (2.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.789 (1.028, 7.563)
	Treatment P-value [b]		0.03486
	Interaction P-value [c]		0.35446
Skin reactions	No. of Events (%)	27 (13.5)	2 (1.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		13.125 (3.122, 55.176)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.27969

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Any	No. of Events (%)	73 (28.2)	19 (7.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.157 (2.509, 6.887)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.68231
Hyperglycemia	No. of Events (%)	20 (7.7)	4 (1.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.968 (1.698, 14.537)
	Treatment P-value [b]		0.00116
	Interaction P-value [c]		0.99028

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Peripheral Neuropathy	No. of Events (%)	23 (8.9)	9 (3.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.229 (1.031, 4.819)
	Treatment P-value [b]		0.03672
	Interaction P-value [c]		0.51647
Skin reactions	No. of Events (%)	40 (15.4)	5 (2.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		8.290 (3.271, 21.009)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.52686

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: >=3 lines

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Any	No. of Events (%)	6 (16.2)	2 (5.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.928 (0.591, 14.504)
	Treatment P-value [b]		0.17616
	Interaction P-value [c]		0.68231
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]		0.99028

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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: >=3 lines

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=37)	Chemotherapy (N=36)
Peripheral 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]		0.860 (0.054, 13.752)
	Treatment P-value [b]		0.92073
	Interaction P-value [c]		0.51647
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]		3.844 (0.430, 34.398)
	Treatment P-value [b]		0.19089
	Interaction P-value [c]		0.52686

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Responder

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Any	No. of Events (%)	21 (34.4)	2 (4.1)
	Median Survival Est. (95% CI)	NC (20.70, NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		9.620 (2.255, 41.034)
	Treatment P-value [b]		0.00017
	Interaction P-value [c]		0.16989
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]		4.853 (0.584, 40.315)
	Treatment P-value [b]		0.09804
	Interaction P-value [c]		0.93346

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Responder

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=61)	Chemotherapy (N=49)
Peripheral Neuropathy	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]		5.754 (0.719, 46.019)
	Treatment P-value [b]		0.06425
	Interaction P-value [c]		0.22483
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]		0.00564
	Interaction P-value [c]		0.98826

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Any	No. of Events (%)	51 (25.2)	17 (8.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		3.247 (1.875, 5.623)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.16989
Hyperglycemia	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]		4.370 (1.245, 15.336)
	Treatment P-value [b]		0.01256
	Interaction P-value [c]		0.93346

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Peripheral Neuropathy	No. of Events (%)	11 (5.4)	7 (3.5)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		1.398 (0.542, 3.607)
	Treatment P-value [b]		0.48477
	Interaction P-value [c]		0.22483
Skin reactions	No. of Events (%)	33 (16.3)	6 (3.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.770 (2.417, 13.774)
	Treatment P-value [b]		<.00001
	Interaction P-value [c]		0.98826

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable. Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

3.10.4 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)
Any	No. of Events (%)	6 (5.7)	2 (1.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		2.857 (0.577, 14.159)
	Treatment P-value [b]		0.18363
	Interaction P-value [c]		0.43630
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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Any	No. of Events (%)	19 (10.0)	3 (1.6)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		6.351 (1.879, 21.467)
	Treatment P-value [b]		0.00064
	Interaction P-value [c]		0.43630
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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Any	No. of Events (%)	17 (6.9)	3 (1.3)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		5.160 (1.512, 17.610)
	Treatment P-value [b]		0.00355
	Interaction P-value [c]		0.96401
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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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=51)	Chemotherapy (N=65)
Any	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]		5.400 (1.146, 25.437)
	Treatment P-value [b]		0.01581
	Interaction P-value [c]		0.96401
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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Any	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]		5.334 (1.844, 15.428)
	Treatment P-value [b]		0.00054
	Interaction P-value [c]		0.54897
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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

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)
Any	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]		2.390 (0.217, 26.347)
	Treatment P-value [b]		0.47186
	Interaction P-value [c]		0.54897
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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
Table SAESI.KM.S4.SAF: Time to First Serious AESI (Months) (Safety Analysis Set)
Subgroup: Region, Level: Western Europe

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=122)	Chemotherapy (N=123)
Any	No. of Events (%)	13 (10.7)	3 (2.4)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.238 (1.208, 14.876)
	Treatment P-value [b]		0.01498
	Interaction P-value [c]		0.87175

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
Table SAESI.KM.S4.SAF: Time to First Serious AESI (Months) (Safety Analysis Set)
Subgroup: Region, Level: US

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=42)	Chemotherapy (N=39)
Any	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]		0.00816
	Interaction P-value [c]		0.87175

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
Table SAESI.KM.S4.SAF: Time to First Serious 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)
Any	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]		2.441 (0.473, 12.583)
	Treatment P-value [b]		0.25972
	Interaction P-value [c]		0.87175

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
Table SAESI.KM.S5.SAF: Time to First Serious 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)
Any	No. of Events (%)	13 (10.8)	1 (0.8)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		13.774 (1.802, 105.274)
	Treatment P-value [b]		0.00104
	Interaction P-value [c]		0.17904

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
Table SAESI.KM.S5.SAF: Time to First Serious 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)
Any	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]		2.793 (0.900, 8.663)
	Treatment P-value [b]		0.06405
	Interaction P-value [c]		0.17904

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
Table SAESI.KM.S6.SAF: Time to First Serious 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)
Any	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]		9.441 (1.210, 73.700)
	Treatment P-value [b]		0.00845
	Interaction P-value [c]		0.43758

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
Table SAESI.KM.S6.SAF: Time to First Serious 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)
Any	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]		3.749 (1.244, 11.296)
	Treatment P-value [b]		0.01191
	Interaction P-value [c]		0.43758

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
Table SAESI.KM.S7.SAF: Time to First Serious 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)
Any	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]		2.498 (0.687, 9.076)
	Treatment P-value [b]		0.15423
	Interaction P-value [c]		0.42127

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
Table SAESI.KM.S7.SAF: Time to First Serious 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 (%)	9 (10.6)	1 (0.9)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		11.726 (1.485, 92.566)
	Treatment P-value [b]		0.00287
	Interaction P-value [c]		0.42127

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
Table SAESI.KM.S7.SAF: Time to First Serious 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)
Any	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]		6.462 (0.778, 53.676)
	Treatment P-value [b]		0.04638
	Interaction P-value [c]		0.42127

Subgroup analyses are conducted if there exist at least 2 levels with >= 10 patients across treatment arms and >=10 events in total across treatment arms in at least 1 level.
The median is based on Kaplan-Meier estimation. HR and 95% CI are based on a Cox PH model adjusting for treatment. A HR of < 1 favours Enfortumab Vedotin. The Efron method is used to handle tied event times. NA: Not Available. NC: Not Calculable.
Stratification factors are as follows; Region, Liver Metastasis and ECOG PS all as defined by the investigator at randomisation.
[a] Based on a stratified Cox proportional hazards model, unstratified for subgroup analyses.
[b] Based on a 2-sided stratified log-rank test, unstratified for subgroup analyses.
[c] Subgroup analyses include an adjustment for subgroup and treatment*subgroup interaction. Homogeneity test of treatment effects between Pre-selected Investigator's Choice of Chemotherapy.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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: Upper Tract

Adverse Event of Special Interest Type	Statistics	Enfortumab Vedotin (N=96)	Chemotherapy (N=102)
Any	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]		6.377 (0.768, 52.969)
	Treatment P-value [b]		0.05205
	Interaction P-value [c]		0.77242
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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 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)
Any	No. of Events (%)	19 (9.5)	4 (2.1)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.491 (1.527, 13.205)
	Treatment P-value [b]		0.00284
	Interaction P-value [c]		0.77242
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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Any	No. of Events (%)	22 (8.5)	3 (1.2)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		7.251 (2.170, 24.231)
	Treatment P-value [b]		0.00017
	Interaction P-value [c]		0.14001
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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Any	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]		1.428 (0.239, 8.549)
	Treatment P-value [b]		0.68664
	Interaction P-value [c]		0.14001
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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Any	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]		3.134 (0.350, 28.047)
	Treatment P-value [b]		0.29707
	Interaction P-value [c]		0.73254
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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential

Astellas: 7465-CL-0301
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)
Any	No. of Events (%)	19 (9.4)	4 (2.0)
	Median Survival Est. (95% CI)	NC (NC , NC)	NC (NC , NC)
	Hazard Ratio (95% CI) [a]		4.798 (1.632, 14.106)
	Treatment P-value [b]		0.00157
	Interaction P-value [c]		0.73254
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.

SOURCE: X:\Numerus\Studies\AST\AST110\Analysis\Prod\Progs\Tab_SI_KM.SAS
Date/time of run: 06DEC2021 19:58. Data Cut Data: 30JUL2021
Analysis Plan: 29NOV2021 Confidential