Clinical trial results:
Dose-escalating and cohort expansion safety trial of tissue factor specific antibody drug conjugate tisotumab vedotin (HuMax®-TF-ADC) in patients with locally advanced and/or metastatic solid tumors known to express tissue factor

Summary

EudraCT number	2015-001120-29
Trial protocol	GB DK BE HU
Global end of trial date	13 December 2017

Results information

Result version number	v1 (current)
This version publication date	26 December 2018
First version publication date	26 December 2018

Trial information

Trial identification

Sponsor protocol code	GEN702

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02552121
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Genmab A/S
Sponsor organisation address	Kalvebod Brygge 43, Copenhagen V, Denmark, 1560
Public contact	Clinical Trial Information, Genmab A/S, +45 7020 2728, clinicaltrials@genmab.com
Scientific contact	Clinical Trial Information, Genmab A/S, +45 7020 2728, clinicaltrials@genmab.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 December 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 December 2017
Global end of trial reached?	Yes
Global end of trial date	13 December 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To establish the tolerability of HuMax-TF-ADC dosed three times every four weeks (3q4wk) in a mixed population of patients with specified solid tumors.

Protection of trial subjects:

This trial was conducted in compliance with independent ethics committee (IEC)/institutional review board (IRB) and International Council for Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines - including Title 21 Part 56 of the United States of America (USA) Code of Federal Regulations (CFR) relating to IRBs and ICH GCP as described in the US Food and Drug Administration (FDA) CFR (21 CFR Part 50, 56, 312), in accordance with applicable regulations regarding clinical safety data management (E2A, E2B(R3)), European Community directives 2001/20, 2001/83, 2003/94 and 2005/28 as enacted into local law, and with ICH guidelines regarding scientific integrity (E4, E8, E9 and E10). In addition, this trial adhered to all local regulatory requirements and requirements for data protection.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 October 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 4
Country: Number of subjects enrolled	United Kingdom: 11
Country: Number of subjects enrolled	Belgium: 13
Country: Number of subjects enrolled	Denmark: 5
Worldwide total number of subjects	33
EEA total number of subjects	29

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0

Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	25
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

For the Dose Escalation, participants took part in the trial at 3 sites located in Denmark, the United Kingdom (UK), and the United States (USA) from 30 Nov 2015 until 10 Feb 2017. Cohort Expansion trial was performed at 10 sites located in Belgium, UK, Denmark, and the USA, from 16 Feb 2016 until the last patient visit on 13 Dec 2017.

Pre-assignment

Screening details:

Participants reported to the clinical study site for the eligibility screening within 21 days prior to the first study drug administration. 20 participants were screened and 9 were enrolled across 3 sites in Part 1 Dose Escalation. 51 participants were screened and 24 were enrolled across 10 sites for Part 2 Cohort Expansion.

Period 1

Period 1 title	Part 1 and Part 2: Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg

Arm description:

Tisotumab vedotin 0.9 mg/kg was administered as an intravenous infusion, over a minimum of 30 minutes, 3 times every 4 weeks (3q4wk).

Arm type	Experimental
Investigational medicinal product name	Tisotumab vedotin
Investigational medicinal product code	
Other name	HuMax®-TF-ADC
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received 0.9 mg/kg or 1.2 mg/kg intravenous infusion, over a minimum of 30 minutes, 3q4wk.

Arm title	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg

Arm description:

Tisotumab vedotin 1.2 mg/kg was administered as an intravenous infusion, over a minimum of 30 minutes, 3q4wk.

Arm type	Experimental
Investigational medicinal product name	Tisotumab vedotin
Investigational medicinal product code	
Other name	HuMax®-TF-ADC
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received 0.9 mg/kg or 1.2 mg/kg intravenous infusion, over a minimum of 30 minutes, 3q4wk.

Arm title	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian

Arm description:

Participants with the indication of ovarian cancer, received Tisotumab vedotin 1.2 mg/kg (the recommended dose for phase II trials [RP2D] from the Dose Escalation part), administered as an intravenous infusion, over a minimum of 30 minutes, 3q4wk.

Arm type	Experimental
Investigational medicinal product name	Tisotumab vedotin
Investigational medicinal product code	
Other name	HuMax®-TF-ADC
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received 1.2 mg/kg, the RP2D from the Dose Escalation phase, intravenous infusion over a minimum of 30 minutes 3q4wk. Due to the observed severe ocular toxicity, participants received 2.0 mg/kg intravenous infusion over a minimum of 30 minutes, once every 3 weeks (1q3w).

Arm title	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical

Arm description:

Participants with the indication of cervical cancer, received Tisotumab vedotin 1.2 mg/kg (RP2D from the Dose Escalation part), administered as an intravenous infusion, over a minimum of 30 minutes, 3q4wk.

Arm type	Experimental
Investigational medicinal product name	Tisotumab vedotin
Investigational medicinal product code	
Other name	HuMax®-TF-ADC
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received 1.2 mg/kg, the RP2D from the Dose Escalation phase, intravenous infusion over a minimum of 30 minutes 3q4wk. Due to the observed severe ocular toxicity, participants received 2.0 mg/kg intravenous infusion over a minimum of 30 minutes, 1q3w.

Arm title	Part 2: Cohort Expansion: Cohort 3 3q4wk - 1q3w Ovarian

Arm description:

Participants with the indication of ovarian cancer, received Tisotumab vedotin 1.2 mg/kg (RP2D from the Dose Escalation part), administered as an intravenous infusion, over a minimum of 30 minutes, 3q4wk. Due to severe ocular toxicity at the dosing schedule of 1.2 mg/kg 3q4wk, participants switched to receive Tisotumab vedotin at 2.0 mg/kg, administered as an intravenous infusion, over a minimum of 30 minutes, 1q3w.

Arm type	Experimental
Investigational medicinal product name	Tisotumab vedotin
Investigational medicinal product code	
Other name	HuMax®-TF-ADC
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received 1.2 mg/kg, the RP2D from the Dose Escalation phase, intravenous infusion over a minimum of 30 minutes 3q4wk. Due to the observed severe ocular toxicity at the dosing schedule of 1.2 mg/kg 3q4wk, participants switched 2.0 mg/kg intravenous infusion over a minimum of 30 minutes, 1q3w.

Arm title	Part 2: Cohort Expansion: Cohort 4 3q4wk - 1q3w Cervical

Arm description:

Participants with the indication of cervical cancer, received Tisotumab vedotin 1.2 mg/kg (RP2D from the Dose Escalation part), administered as an intravenous infusion, over a minimum of 30 minutes, 3q4wk. Due to severe ocular toxicity at the dosing schedule of 1.2 mg/kg 3q4wk, participants switched to receive Tisotumab vedotin at 2.0 mg/kg, administered as an intravenous infusion, over a minimum of 30 minutes, 1q3w.

Arm type	Experimental

Investigational medicinal product name	Tisotumab vedotin
Investigational medicinal product code	
Other name	HuMax®-TF-ADC
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received 1.2 mg/kg, the RP2D from the Dose Escalation phase, intravenous infusion over a minimum of 30 minutes 3q4wk. Due to the observed severe ocular toxicity at the dosing schedule of 1.2 mg/kg 3q4wk, participants switched 2.0 mg/kg intravenous infusion over a minimum of 30 minutes, 1q3w.

Arm title	Part 2: Cohort Expansion: Cohort 5 1q3w Ovarian

Arm description:

Participants with the indication of ovarian cancer received Tisotumab vedotin 2.0 mg/kg, administered as an intravenous infusion, over a minimum of 30 minutes, 1q3w; the revised dose and schedule due to severe ocular toxicity observed at 1.2 mg/kg 3q4wk.

Arm type	Experimental
Investigational medicinal product name	Tisotumab vedotin
Investigational medicinal product code	
Other name	HuMax®-TF-ADC
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received 2.0 mg/kg intravenous infusion over a minimum of 30 minutes, 1q3w.

Arm title	Part 2: Cohort Expansion: Cohort 6 1q3w Cervical

Arm description:

Participants with the indication of cervical cancer, received Tisotumab vedotin 2.0 mg/kg, administered as an intravenous infusion, over a minimum of 30 minutes, 1q3w; the revised dose and schedule due to severe ocular toxicity observed at 1.2 mg/kg 3q4wk.

Arm type	Experimental
Investigational medicinal product name	Tisotumab vedotin
Investigational medicinal product code	
Other name	HuMax®-TF-ADC
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received 2.0 mg/kg intravenous infusion over a minimum of 30 minutes, 1q3w.

Number of subjects in period 1	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian
Started	3	6	11
Completed	0	0	0
Not completed	3	6	11
Adverse event, non-fatal	1	-	6
Patient Choice	-	1	1
Death	-	-	1
Investigator Judgment	-	2	-
Miscellaneous	-	1	-
Disease Progression	2	2	3

Number of subjects in period 1	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical	Part 2: Cohort Expansion: Cohort 3 3q4wk - 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 4 3q4wk - 1q3w Cervical
Started	3	1	5
Completed	0	0	1
Not completed	3	1	4
Adverse event, non-fatal	1	-	-
Patient Choice	-	-	-
Death	-	-	-
Investigator Judgment	-	-	-
Miscellaneous	-	-	-
Disease Progression	2	1	4

Number of subjects in period 1	Part 2: Cohort Expansion: Cohort 5 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 6 1q3w Cervical
Started	1	3
Completed	0	0
Not completed	1	3
Adverse event, non-fatal	-	-
Patient Choice	1	-
Death	-	-
Investigator Judgment	-	-
Miscellaneous	-	-
Disease Progression	-	3

Baseline characteristics

Reporting groups	
Reporting group title	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg
Reporting group description:	
Tisotumab vedotin 0.9 mg/kg was administered as an intravenous infusion, over a minimum of 30 minutes, 3 times every 4 weeks (3q4wk).	
Reporting group title	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg
Reporting group description:	
Tisotumab vedotin 1.2 mg/kg was administered as an intravenous infusion, over a minimum of 30 minutes, 3q4wk.	
Reporting group title	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian
Reporting group description:	
Participants with the indication of ovarian cancer, received Tisotumab vedotin 1.2 mg/kg (the recommended dose for phase II trials [RP2D] from the Dose Escalation part), administered as an intravenous infusion, over a minimum of 30 minutes, 3q4wk.	
Reporting group title	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical
Reporting group description:	
Participants with the indication of cervical cancer, received Tisotumab vedotin 1.2 mg/kg (RP2D from the Dose Escalation part), administered as an intravenous infusion, over a minimum of 30 minutes, 3q4wk.	
Reporting group title	Part 2: Cohort Expansion: Cohort 3 3q4wk - 1q3w Ovarian
Reporting group description:	
Participants with the indication of ovarian cancer, received Tisotumab vedotin 1.2 mg/kg (RP2D from the Dose Escalation part), administered as an intravenous infusion, over a minimum of 30 minutes, 3q4wk. Due to severe ocular toxicity at the dosing schedule of 1.2 mg/kg 3q4wk, participants switched to receive Tisotumab vedotin at 2.0 mg/kg, administered as an intravenous infusion, over a minimum of 30 minutes, 1q3w.	
Reporting group title	Part 2: Cohort Expansion: Cohort 4 3q4wk - 1q3w Cervical
Reporting group description:	
Participants with the indication of cervical cancer, received Tisotumab vedotin 1.2 mg/kg (RP2D from the Dose Escalation part), administered as an intravenous infusion, over a minimum of 30 minutes, 3q4wk. Due to severe ocular toxicity at the dosing schedule of 1.2 mg/kg 3q4wk, participants switched to receive Tisotumab vedotin at 2.0 mg/kg, administered as an intravenous infusion, over a minimum of 30 minutes, 1q3w.	
Reporting group title	Part 2: Cohort Expansion: Cohort 5 1q3w Ovarian
Reporting group description:	
Participants with the indication of ovarian cancer received Tisotumab vedotin 2.0 mg/kg, administered as an intravenous infusion, over a minimum of 30 minutes, 1q3w; the revised dose and schedule due to severe ocular toxicity observed at 1.2 mg/kg 3q4wk.	
Reporting group title	Part 2: Cohort Expansion: Cohort 6 1q3w Cervical
Reporting group description:	
Participants with the indication of cervical cancer, received Tisotumab vedotin 2.0 mg/kg, administered as an intravenous infusion, over a minimum of 30 minutes, 1q3w; the revised dose and schedule due to severe ocular toxicity observed at 1.2 mg/kg 3q4wk.	

Reporting group values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian
Number of subjects	3	6	11
Age categorical Units: Subjects			
Adults (18-64 years)	0	3	10
From 65-84 years	3	3	1

Age continuous			
Units: years			
median	69.0	61	59.0
full range (min-max)	66.0 to 70.0	38.0 to 71.0	50.0 to 65.0
Gender categorical			
Units: Subjects			
Female	1	4	11
Male	2	2	0
Race			
Units: Subjects			
White	3	5	10
Asian	0	1	1
Ethnicity			
Units: Subjects			
Hispanic or Latino	0	0	1
Not Hispanic or Latino	3	6	10
Weight			
Units: kg			
median	80.0	67.5	66.8
full range (min-max)	76.3 to 80.0	48.1 to 85.0	40.0 to 89.6
Height			
Units: cm			
median	171.0	162.0	159.0
full range (min-max)	168.0 to 171.4	156.0 to 175.0	154.0 to 174.0
Body Mass Index (BMI)			
Units: kg/m^2			
median	27.4	25.5	26.4
full range (min-max)	26.0 to 28.3	19.8 to 27.8	16.9 to 32.5

Reporting group values	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical	Part 2: Cohort Expansion: Cohort 3 3q4wk - 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 4 3q4wk - 1q3w Cervical
Number of subjects	3	1	5
Age categorical			
Units: Subjects			
Adults (18-64 years)	3	1	4
From 65-84 years	0	0	1
Age continuous			
Units: years			
median	55.0	46.0	48.0
full range (min-max)	50.0 to 58.0	46.0 to 46.0	39.0 to 67.0
Gender categorical			
Units: Subjects			
Female	3	1	5
Male	0	0	0
Race			
Units: Subjects			
White	3	1	5
Asian	0	0	0
Ethnicity			
Units: Subjects			

Hispanic or Latino	0	0	0
Not Hispanic or Latino	3	1	5

Weight			
Units: kg			
median	55.2	57.8	72.0
full range (min-max)	41.7 to 63.5	57.8 to 57.8	52.8 to 79.3
Height			
Units: cm			
median	157.0	160.6	168.0
full range (min-max)	148.0 to 161.0	160.6 to 160.6	159 to 177.8
Body Mass Index (BMI)			
Units: kg/m^2			
median	22.4	22.4	24.0
full range (min-max)	16.1 to 29.0	22.4 to 22.4	18.7 to 28.5

Reporting group values	Part 2: Cohort Expansion: Cohort 5 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 6 1q3w Cervical	Total
Number of subjects	1	3	33
Age categorical			
Units: Subjects			
Adults (18-64 years)	1	3	25
From 65-84 years	0	0	8
Age continuous			
Units: years			
median	59.0	48.0	
full range (min-max)	59.0 to 59.0	30.0 to 60.0	-
Gender categorical			
Units: Subjects			
Female	1	3	29
Male	0	0	4
Race			
Units: Subjects			
White	1	3	31
Asian	0	0	2
Ethnicity			
Units: Subjects			
Hispanic or Latino	0	0	1
Not Hispanic or Latino	1	3	32
Weight			
Units: kg			
median	96.8	65.3	
full range (min-max)	96.8 to 96.8	60.5 to 65.5	-
Height			
Units: cm			
median	170.5	161.0	
full range (min-max)	170.5 to 170.5	156.0 to 162.0	-
Body Mass Index (BMI)			
Units: kg/m^2			
median	33.3	24.9	
full range (min-max)	33.3 to 33.3	23.3 to 26.9	-

End points

End points reporting groups

Reporting group title	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg
Reporting group description:	
Tisotumab vedotin 0.9 mg/kg was administered as an intravenous infusion, over a minimum of 30 minutes, 3 times every 4 weeks (3q4wk).	

Reporting group title	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg
Reporting group description:	
Tisotumab vedotin 1.2 mg/kg was administered as an intravenous infusion, over a minimum of 30 minutes, 3q4wk.	

Reporting group title	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian
Reporting group description:	
Participants with the indication of ovarian cancer, received Tisotumab vedotin 1.2 mg/kg (the recommended dose for phase II trials [RP2D] from the Dose Escalation part), administered as an intravenous infusion, over a minimum of 30 minutes, 3q4wk.	

Reporting group title	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical
Reporting group description:	
Participants with the indication of cervical cancer, received Tisotumab vedotin 1.2 mg/kg (RP2D from the Dose Escalation part), administered as an intravenous infusion, over a minimum of 30 minutes, 3q4wk.	

Reporting group title	Part 2: Cohort Expansion: Cohort 3 3q4wk - 1q3w Ovarian
Reporting group description:	
Participants with the indication of ovarian cancer, received Tisotumab vedotin 1.2 mg/kg (RP2D from the Dose Escalation part), administered as an intravenous infusion, over a minimum of 30 minutes, 3q4wk. Due to severe ocular toxicity at the dosing schedule of 1.2 mg/kg 3q4wk, participants switched to receive Tisotumab vedotin at 2.0 mg/kg, administered as an intravenous infusion, over a minimum of 30 minutes, 1q3w.	

Reporting group title	Part 2: Cohort Expansion: Cohort 4 3q4wk - 1q3w Cervical
Reporting group description:	
Participants with the indication of cervical cancer, received Tisotumab vedotin 1.2 mg/kg (RP2D from the Dose Escalation part), administered as an intravenous infusion, over a minimum of 30 minutes, 3q4wk. Due to severe ocular toxicity at the dosing schedule of 1.2 mg/kg 3q4wk, participants switched to receive Tisotumab vedotin at 2.0 mg/kg, administered as an intravenous infusion, over a minimum of 30 minutes, 1q3w.	

Reporting group title	Part 2: Cohort Expansion: Cohort 5 1q3w Ovarian
Reporting group description:	
Participants with the indication of ovarian cancer received Tisotumab vedotin 2.0 mg/kg, administered as an intravenous infusion, over a minimum of 30 minutes, 1q3w; the revised dose and schedule due to severe ocular toxicity observed at 1.2 mg/kg 3q4wk.	

Reporting group title	Part 2: Cohort Expansion: Cohort 6 1q3w Cervical
Reporting group description:	
Participants with the indication of cervical cancer, received Tisotumab vedotin 2.0 mg/kg, administered as an intravenous infusion, over a minimum of 30 minutes, 1q3w; the revised dose and schedule due to severe ocular toxicity observed at 1.2 mg/kg 3q4wk.	

Primary: Part 1: Number of Participants who Experience at Least One Adverse Event (AE)

End point title	Part 1: Number of Participants who Experience at Least One Adverse Event (AE)[1][2]
End point description:	
An Adverse Event (AE) is defined as any untoward medical occurrence in a clinical investigation participant administered a drug; it does not necessarily have to have a causal relationship with this treatment. A treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset that occurs after receiving study drug.	

End point type	Primary

End point timeframe:

Part 1 Dose Escalation Phase: Baseline to end of trial, a maximum of 24 weeks (+/- 7 days) post last dose.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical tests were performed for this trial

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: Participants	3	6		

Statistical analyses

No statistical analyses for this end point

Primary: Part 2: Number of Participants who Experience at Least One Adverse Event (AE)

End point title	Part 2: Number of Participants who Experience at Least One Adverse Event (AE)[3][4]

End point description:

An Adverse Event (AE) is defined as any untoward medical occurrence in a clinical investigation participant administered a drug; it does not necessarily have to have a causal relationship with this treatment. A treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset that occurs after receiving study drug.

End point type	Primary

End point timeframe:

Part 2 Cohort Expansion: Baseline to end of trial, approximately 36 weeks.

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical tests were performed for this trial

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 2 is displayed for this endpoint.

End point values	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical	Part 2: Cohort Expansion: Cohort 3 3q4wk - 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 4 3q4wk - 1q3w Cervical
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	3	1	5
Units: Participants	11	3	1	5

End point values	Part 2: Cohort Expansion: Cohort 5 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 6 1q3w Cervical		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	3		
Units: Participants	0	3		

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Number of Participants who Experienced at Least One or More Serious Adverse Event (SAE)

End point title	Part 1: Number of Participants who Experienced at Least One or More Serious Adverse Event (SAE)[5][6]

End point description:

End point type	Primary

End point timeframe:

Part 1 Dose Escalation: Baseline to end of trial, maximum of 24 weeks (+/- 7 days) post last dose.

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical tests were performed for this trial.

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: Participants	1	2		

Statistical analyses

No statistical analyses for this end point

Primary: Part 2: Number of Participants who Experienced at Least One or More Serious Adverse Event (SAE)

End point title	Part 2: Number of Participants who Experienced at Least One or More Serious Adverse Event (SAE)[7][8]

End point description:

End point type	Primary

End point timeframe:

Part 2 Cohort Expansion: Baseline to end of trial, up to 36 weeks.

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical tests were performed for this trial

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 2 is displayed for this endpoint.

End point values	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical	Part 2: Cohort Expansion: Cohort 3 3q4wk - 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 4 3q4wk - 1q3w Cervical
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	3	1	5
Units: Participants	9	2	0	2

End point values	Part 2: Cohort Expansion: Cohort 5 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 6 1q3w Cervical		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	3		
Units: Participants	0	1		

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Number of Participants who Experienced at Least One or More Infusion-related Adverse Events

End point title	Part 1: Number of Participants who Experienced at Least One or More Infusion-related Adverse Events[9][10]

End point description:

An infusion-related AE was defined as an AE occurring during infusion where the onset date and time of the event occurred within infusion time (+24 hours), and the event was judged as related to Tisotumab vedotin by the investigator.

End point type	Primary

End point timeframe:

Part 1 Dose Escalation: Day 1, Day 8 & Day 15 (+1 day) until end of treatment, up to 48 weeks.

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical tests were performed for this trial

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: Participants	2	4		

Statistical analyses

No statistical analyses for this end point

Primary: Part 2: Number of Participants who Experienced at Least One or More Infusion-related Adverse Events

End point title	Part 2: Number of Participants who Experienced at Least One or More Infusion-related Adverse Events[11][12]

End point description:

An infusion-related AE was defined as an AE occurring during infusion where the onset date and time of the event occurred within infusion time (+24 hours), and the event was judged as related to Tisotumab vedotin by the investigator.

End point type	Primary

End point timeframe:

Part 2 Cohort Expansion: Day 1, Day 8 & Day 15 (+1 day) until end of trial, up to 36 weeks.

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical tests were performed for this trial

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 2 is displayed for this endpoint.

End point values	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical	Part 2: Cohort Expansion: Cohort 3 3q4wk - 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 4 3q4wk - 1q3w Cervical
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	3	1	5
Units: Participants	4	2	1	1

End point values	Part 2: Cohort Expansion: Cohort 5 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 6 1q3w Cervical		

Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	3		
Units: Participants	0	1		

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Number of Participants who Experienced at Least One or More Common Terminology Criteria for Adverse Events (CTCAE) Grade >=3 Adverse Events

End point title	Part 1: Number of Participants who Experienced at Least One or More Common Terminology Criteria for Adverse Events (CTCAE) Grade >=3 Adverse Events[13][14]

End point description:

End point type	Primary

End point timeframe:

Part 1 Dose Escalation: Baseline to end of trial, a maximum of 24 weeks (+/- 7 days) post last dose.

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.
[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: Participants	1	3		

Statistical analyses

No statistical analyses for this end point

Primary: Part 2: Number of Participants who Experienced at Least One or More Common Terminology Criteria for Adverse Events (CTCAE) Grade >=3 Adverse Events

End point title	Part 2: Number of Participants who Experienced at Least One or More Common Terminology Criteria for Adverse Events (CTCAE) Grade >=3 Adverse Events[15][16]

End point description:

End point type	Primary

End point timeframe:

Part 2 Cohort Expansion: Baseline to end of trial, up to 36 weeks.

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 2 is displayed for this endpoint.
[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 2 is displayed for this endpoint.

End point values	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical	Part 2: Cohort Expansion: Cohort 3 3q4wk - 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 4 3q4wk - 1q3w Cervical
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	3	1	5
Units: Participants	10	2	0	3

End point values	Part 2: Cohort Expansion: Cohort 5 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 6 1q3w Cervical		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	3		
Units: Participants	0	1		

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Number of Participants who Experienced at Least One or More Treatment-related Adverse Event

End point title	Part 1: Number of Participants who Experienced at Least One or More Treatment-related Adverse Event[17][18]

End point description:

End point type	Primary

End point timeframe:

Part 1 Dose Escalation: Baseline to end of trial, a maximum of 24 weeks (+/- 7 days) post last dose.

Notes:

[17] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical tests were performed for this trial

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: Participants	3	6		

Statistical analyses

No statistical analyses for this end point

Primary: Part 2: Number of Participants who Experienced at Least One or More Treatment-related Adverse Event

End point title	Part 2: Number of Participants who Experienced at Least One or More Treatment-related Adverse Event[19][20]

End point description:

End point type	Primary

End point timeframe:

Part 2 Cohort Expansion: Baseline to end of trial, up to 36 weeks.

Notes:

[19] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical tests were performed for this trial

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 2 is displayed for this endpoint.

End point values	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical	Part 2: Cohort Expansion: Cohort 3 3q4wk - 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 4 3q4wk - 1q3w Cervical
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	3	1	5
Units: Participants	9	3	1	5

End point values	Part 2: Cohort Expansion: Cohort 5 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 6 1q3w Cervical		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	3		
Units: Participants	0	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Number of Participants with Markedly Abnormal Laboratory Values

End point title	Part 1: Number of Participants with Markedly Abnormal Laboratory Values [21]

End point description:

The number of participants with any markedly abnormal standard safety laboratory values collected throughout study. Markedly abnormal laboratory values are defined as any grade >=3 laboratory abnormality events.

End point type	Secondary

End point timeframe:

Part 1 Dose Escalation: Baseline to end of trial, a maximum of 24 weeks (+/- 7 days) post last dose.

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: Participants	0	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Number of Participants with Markedly Abnormal Laboratory Values

End point title	Part 2: Number of Participants with Markedly Abnormal Laboratory Values[22]

End point description:

The number of participants with any markedly abnormal standard safety laboratory values collected throughout study. Markedly abnormal laboratory values are defined as any grade >=3 laboratory abnormality events.

End point type	Secondary

End point timeframe:

Part 2 Cohort Expansion: Baseline to end of trial, up to 36 weeks.

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 2 is displayed for this endpoint.

End point values	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical	Part 2: Cohort Expansion: Cohort 3 3q4wk - 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 4 3q4wk - 1q3w Cervical
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	3	1	5
Units: Participants	5	2	0	3

End point values	Part 2: Cohort Expansion: Cohort 5 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 6 1q3w Cervical		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	3		
Units: Participants	1	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Number of Participants who Experienced a Skin Rash

End point title	Part 1: Number of Participants who Experienced a Skin Rash[23]

End point description:

End point type	Secondary

End point timeframe:

Part 1 Dose Escalation: Baseline to end of trial, a maximum of 24 weeks (+/- 7 days) post last dose.

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: Participants	0	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Number of Participants who Experienced a Skin Rash

End point title	Part 2: Number of Participants who Experienced a Skin Rash[24]

End point description:

End point type	Secondary

End point timeframe:

Cohort Expansion: Baseline to end of trial, up to 36 weeks.

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 2 is displayed for this endpoint.

End point values	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical	Part 2: Cohort Expansion: Cohort 3 3q4wk - 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 4 3q4wk - 1q3w Cervical
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	3	1	5
Units: Participants	2	0	1	1

End point values	Part 2: Cohort Expansion: Cohort 5 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 6 1q3w Cervical		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	3		
Units: Participants	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Number of Participants who Experienced a Bleeding Event

End point title	Part 1: Number of Participants who Experienced a Bleeding Event[25]

End point description:

End point type	Secondary

End point timeframe:

Part 1 Dose Escalation: Baseline until end of treatment, up to 48 weeks.

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: Participants	3	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Number of Participants who Experienced a Bleeding Event

End point title	Part 2: Number of Participants who Experienced a Bleeding Event[26]

End point description:

End point type	Secondary

End point timeframe:

Part 2 Cohort Expansion: Baseline to end of trial, up to 36 weeks.

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 2 is displayed for this endpoint.

End point values	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical	Part 2: Cohort Expansion: Cohort 3 3q4wk - 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 4 3q4wk - 1q3w Cervical
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	3	1	5
Units: Participants	7	3	1	5

End point values	Part 2: Cohort Expansion: Cohort 5 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 6 1q3w Cervical		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	3		
Units: Participants	0	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Number of Participants who Experienced a Neuropathy Event

End point title	Part 1: Number of Participants who Experienced a Neuropathy Event[27]

End point description:

End point type	Secondary

End point timeframe:

Part 1 Dose Escalation: Baseline until end of treatment, up to 48 weeks.

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: Participants	1	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Number of Participants who Experienced a Neuropathy Event

End point title	Part 2: Number of Participants who Experienced a Neuropathy Event[28]

End point description:

End point type	Secondary

End point timeframe:

Part 2 Cohort Expansion: Baseline to end of trial, up to 36 weeks.

Notes:

[28] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 2 is displayed for this endpoint.

End point values	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical	Part 2: Cohort Expansion: Cohort 3 3q4wk - 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 4 3q4wk - 1q3w Cervical
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	3	1	5
Units: Participants	3	1	0	2

End point values	Part 2: Cohort Expansion: Cohort 5 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 6 1q3w Cervical		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	3		
Units: Participants	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: AUC0-t: Area Under the Plasma Concentration-Time Curve From Time 0 to the Time of Last Quantifiable Concentration for Tisotumab vedotin (HuMax-TF-ADC)

End point title	Part 1: AUC0-t: Area Under the Plasma Concentration-Time Curve From Time 0 to the Time of Last Quantifiable Concentration for Tisotumab vedotin (HuMax-TF-ADC)[29]

End point description:

End point type	Secondary

End point timeframe:

Part 1 Dose Escalation: Baseline to end of treatment, up to 48 weeks.

Notes:

[29] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: h*µg/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	3336 (± 7.3)	5317 (± 34.6)		
Cycle 1 Day 1	867 (± 17.6)	1328 (± 48.0)		
Cycle 1 Day 8	1603 (± 16.2)	2216 (± 11.7)		
Cycle 1 Day 15	789 (± 15.6)	1411 (± 94.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: AUC0-t: Area Under the Plasma Concentration-Time Curve From Time 0 to the Time of Last Quantifiable Concentration for Tisotumab vedotin (HuMax-TF-ADC)

End point title	Part 2: AUC0-t: Area Under the Plasma Concentration-Time Curve From Time 0 to the Time of Last Quantifiable Concentration for Tisotumab vedotin (HuMax-TF-ADC)[30]

End point description:

9999 has been recorded when there is no data available for the data point. Arms only included 1 participant, no Geometric Coefficient of Variation could be calculated.

End point type	Secondary

End point timeframe:

Part 2 Cohort Expansion: Baseline to end of trial, up to 36 weeks

Notes:

[30] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 2 is displayed for this endpoint.

End point values	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[31]	3[32]		
Units: h*µg/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	2267 (± 24.8)	1755 (± 19.1)		
Cycle 1 Dose 1	1889 (± 29.3)	1412 (± 11.9)		
Cycle 1 Dose 2	150 (± 56.2)	123 (± 85.4)		
Cycle 1 Dose 3	410 (± 26.4)	204 (± 71.3)		

Notes:

[31] - Cycle 1 Dose 2: n = 9
Cycle 1 Dose 3: n = 6
[32] - Cycle 1 Dose 3: n = 2

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: AUCinf: Area Under the Plasma Concentration-time Curve from Time 0 to Infinity for Tisotumab vedotin (HuMax-TF-ADC)

End point title	Part 1: AUCinf: Area Under the Plasma Concentration-time Curve from Time 0 to Infinity for Tisotumab vedotin (HuMax-TF-ADC)[33]

End point description:

End point type	Secondary

End point timeframe:

Part 1 Dose Escalation: Baseline until end of treatment, up to 48 weeks.

Notes:

[33] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	4		
Units: h*µg/mL				
geometric mean (geometric coefficient of variation)	920 (± 3.6)	1106 (± 21.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Cmax: Maximum Observed Plasma Concentration for Tisotumab vedotin (HuMax-TF-ADC)

End point title	Part 1: Cmax: Maximum Observed Plasma Concentration for Tisotumab vedotin (HuMax-TF-ADC)[34]

End point description:

End point type	Secondary

End point timeframe:

Part 1 Dose Escalation: Baseline to end of trial, up to 48 weeks.

Notes:

[34] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: µg/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	21.2 (± 14.5)	30.7 (± 10.1)		
Cycle 1 Day 1	20.2 (± 17.9)	28.7 (± 12.1)		
Cycle 1 Day 8	20.9 (± 14.1)	28.0 (± 8.9)		
Cycle 1 Day 15	19.9 (± 11.8)	26.8 (± 21.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Cmax: Maximum Observed Plasma Concentration for Tisotumab vedotin (HuMax-TF-ADC)

End point title	Part 2: Cmax: Maximum Observed Plasma Concentration for Tisotumab vedotin (HuMax-TF-ADC)[35]

End point description:

9999 has been recorded when there is no data available for the data point. Arms only included 1 participant, no Geometric Coefficient of Variation could be calculated.

9999 has been entered For Arms 'Part 2 Cohort Expansion: Cohort 5 1q3w Ovarian' and 'Part 2 Cohort Expansion: Cohort 6 1q3w Cervical'; as data is only available at Cycle 1 due to changes in dosing schedule. Participants in these arms are only dosed once every 3 weeks (1q3wk).

End point type	Secondary

End point timeframe:

Part 2 Cohort Expansion: Baseline to end of trial, up to 36 weeks.

Notes:

[35] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 2 is displayed for this endpoint.

End point values	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[36]	3[37]		
Units: µg/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	28.2 (± 34.5)	19.5 (± 17.6)		
Cycle 1 Dose 1	28.2 (± 34.5)	19.5 (± 17.6)		
Cycle 1 Dose 2	1.00 (± 42.0)	1.13 (± 112.2)		
Cycle 1 Dose 3	3.85 (± 24.5)	1.85 (± 77.6)		

Notes:

[36] - Cycle 1 Dose 2: n = 9
Cycle 1 Dose 3: n = 6
[37] - Cycle 1 Dose 3: n = 2

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Tmax: Time to Reach the Maximum Plasma Concentration for Tisotumab vedotin (HuMax-TF-ADC)

End point title	Part 1: Tmax: Time to Reach the Maximum Plasma

	Concentration for Tisotumab vedotin (HuMax-TF-ADC)[38]

End point description:

End point type	Secondary

End point timeframe:

Part 1 Dose Escalation: Baseline to end of treatment, up to 48 weeks.

Notes:

[38] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: hours				
geometric mean (geometric coefficient of variation)				
Cycle 1	5.864 (± 172.022)	5.061 (± 166.177)		
Cycle 1 Day 1	0.747 (± 11.547)	0.873 (± 79.228)		
Cycle 1 Day 8	0.717 (± 0)	0.846 (± 86.481)		
Cycle 1 Day 15	1.141 (± 81.075)	1.084 (± 73.110)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Tmax: Time to Reach the Maximum Plasma Concentration for Tisotumab vedotin (HuMax-TF-ADC)

End point title	Part 2: Tmax: Time to Reach the Maximum Plasma Concentration for Tisotumab vedotin (HuMax-TF-ADC)[39]

End point description:

9999 has been recorded when there is no data available for the data point. Arms only included 1 participant, no Geometric Coefficient of Variation could be calculated.

9999 has been entered For Arms 'Part 2 Cohort Expansion: Cohort 5 1q3w Ovarian' and 'Part 2 Cohort Expansion: Cohort 6 1q3w Cervical'; as data is only available at Cycle 1 due to changes in dosing schedule. Participants in these arms are only dosed once every 3 weeks (1q3wk).

End point type	Secondary

End point timeframe:

Part 2 Cohort Expansion: Baseline to end of trial, up to 36 weeks.

Notes:

[39] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only

data for Part 2 is displayed for this endpoint.

End point values	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[40]	3[41]		
Units: hours				
geometric mean (geometric coefficient of variation)				
Cycle 1	0.75 (± 68.49)	0.58 (± 22.85)		
Cycle 1 Dose 1	0.75 (± 68.49)	0.58 (± 22.85)		
Cycle 1 Dose 2	165.06 (± 75.01)	106.93 (± 55.38)		
Cycle 1 Dose 3	71.23 (± 24.35)	80.37 (± 20.24)		

Notes:

[40] - Cycle 1 Dose 2: n = 9
Cycle 1 Dose 3: n = 6
[41] - Cycle 1 Dose 3: n = 2

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Terminal Phase Elimination Half-life (T1/2) for Tisotumab vedotin (HuMax-TF-ADC)

End point title	Part 1: Terminal Phase Elimination Half-life (T1/2) for Tisotumab vedotin (HuMax-TF-ADC)[42]

End point description:

End point type	Secondary

End point timeframe:

Part 1 Dose Escalation: Baseline to end of treatment, up to 48 weeks.

Notes:

[42] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	4		
Units: hours				
geometric mean (geometric coefficient of variation)	40.45 (± 24.78)	48.15 (± 16.47)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Total Clearance (CL) of Tisotumab vedotin (HuMax-TF-ADC)

End point title	Part 1: Total Clearance (CL) of Tisotumab vedotin (HuMax-TF-ADC)[43]

End point description:

End point type	Secondary

End point timeframe:

Part 1 Dose Escalation: Baseline to end of treatment, up to 48 weeks.

Notes:

[43] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	4		
Units: mL/h/kg				
geometric mean (geometric coefficient of variation)	0.979 (± 3.561)	1.085 (± 21.476)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Apparent Volume of Distribution (Vz) for Tisotumab vedotin (HuMax-TF-ADC)

End point title	Part 1: Apparent Volume of Distribution (Vz) for Tisotumab vedotin (HuMax-TF-ADC)[44]

End point description:

End point type	Secondary

End point timeframe:

Part 1 Dose Escalation: Baseline to end of treatment, up to 48 weeks.

Notes:

[44] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	4		
Units: mL/kg				
geometric mean (geometric coefficient of variation)	66.75 (± 6.67)	75.37 (± 14.89)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Trough Concentration (Ctrough) Steady State Plasma Pharmacokinetic for Tisotumab vedotin (HuMax-TF-ADC)

End point title	Part 1: Trough Concentration (Ctrough) Steady State Plasma Pharmacokinetic for Tisotumab vedotin (HuMax-TF-ADC)[45]

End point description:

End point type	Secondary

End point timeframe:

Part 1 Dose Escalation: Baseline to end of treatment, up to 48 weeks.

Notes:

[45] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1	30.0 (± 0)	30.0 (± 0)		
Cycle 1 Day 8	797.3 (± 22.1)	1328.5 (± 191.8)		
Cycle 1 Day 15	912.1 (± 23.7)	989.0 (± 44.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: AUC0-t: Area Under the Plasma Concentration-Time Curve From Time 0 to the Time of Last Quantifiable Concentration for Total HuMax-TF

(Cojugated and Non-conjugated)

End point title	Part 1: AUC0-t: Area Under the Plasma Concentration-Time Curve From Time 0 to the Time of Last Quantifiable Concentration for Total HuMax-TF (Cojugated and Non-conjugated)[46]

End point description:

End point type	Secondary

End point timeframe:

Part 1: Baseline to end of treatment (Part 1), up to 48 weeks

Notes:

[46] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: h*µg/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	3916 (± 7.3)	5573 (± 15.0)		
Cycle 1 Day 1	1058 (± 15.0)	1530 (± 34.7)		
Cycle 1 Day 8	1750 (± 16.2)	2460 (± 8.5)		
Cycle 1 Day 15	1012 (± 25.7)	1426 (± 28.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: AUC0-t: Area Under the Plasma Concentration-Time Curve From Time 0 to the Time of Last Quantifiable Concentration for Total HuMax-TF (Cojugated and Non-conjugated)

End point title	Part 2: AUC0-t: Area Under the Plasma Concentration-Time Curve From Time 0 to the Time of Last Quantifiable Concentration for Total HuMax-TF (Cojugated and Non-conjugated)[47]

End point description:

End point type	Secondary

End point timeframe:

Part 2: Baseline to end of trial (Part 2), up to 36 weeks

Notes:

[47] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 2 is displayed for this endpoint.

End point values	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[48]	3[49]		
Units: h*µg/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	2660 (± 20.0)	1948 (± 35.2)		
Cycle 1 Dose 1	1980 (± 24.5)	460 (± 84.5)		
Cycle 1 Dose 2	299 (± 55.0)	192 (± 80.9)		
Cycle 1 Dose 3	679 (± 25.7)	291 (± 89.9)		

Notes:

[48] - Cycle 1 Dose 2: n = 9
Cycle 1 Dose 3: n = 6
[49] - Cycle 1 Dose 3: n = 2

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: AUCinf: Area Under the Plasma Concentration-time Curve From Time 0 to Infinity for Total HuMax-TF (Cojugated and Non-conjugated)

End point title	Part 1: AUCinf: Area Under the Plasma Concentration-time Curve From Time 0 to Infinity for Total HuMax-TF (Cojugated and Non-conjugated)[50]

End point description:

End point type	Secondary

End point timeframe:

Part 1: Baseline to end of treatment (Part 1), up to 48 weeks

Notes:

[50] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	6		
Units: h*µg/mL				
geometric mean (geometric coefficient of variation)	1268 (± 14.4)	1594 (± 24.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Cmax: Maximum Observed Plasma Concentration for Total HuMax-TF (Cojugated and Non-conjugated)

End point title	Part 1: Cmax: Maximum Observed Plasma Concentration for Total HuMax-TF (Cojugated and Non-conjugated)[51]

End point description:

End point type	Secondary

End point timeframe:

Part 1: Baseline to end of treatment (Part 1), up to 48 weeks

Notes:

[51] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: µg/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	22.1 (± 9.1)	31.7 (± 11.9)		
Cycle 1 Day 1	20.3 (± 14.3)	30.2 (± 11.5)		
Cycle 1 Day 8	21.0 (± 6.3)	29.2 (± 6.6)		
Cycle 1 Day 15	20.9 (± 12.0)	29.2 (± 16.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Cmax: Maximum Observed Plasma Concentration for Total HuMax-TF (Conjugated and Non-conjugated)

End point title	Part 2: Cmax: Maximum Observed Plasma Concentration for Total HuMax-TF (Conjugated and Non-conjugated)[52]

End point description:

End point type	Secondary

End point timeframe:

Part 2: Baseline to end of trial (Part 2) up to 36 weeks

Notes:

[52] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 2 is displayed for this endpoint.

End point values	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[53]	3[54]		
Units: µg/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	27.5 (± 36.4)	20.6 (± 18.6)		
Cycle 1 Dose 1	27.5 (± 36.4)	20.6 (± 18.6)		
Cycle 1 Dose 2	2.00 (± 41.6)	1.91 (± 105.0)		
Cycle 1 Dose 3	6.39 (± 24.6)	3.68 (± 66.1)		

Notes:

[53] - Cycle 1 Dose 2: n = 9
Cycle 1 Dose 3: n = 6
[54] - Cycle 1 Dose 3: n = 2

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Tmax: Time to Reach the Maximum Plasma Concentration for Total HuMax-TF (Cojugated and Non-conjugated)

End point title	Part 1: Tmax: Time to Reach the Maximum Plasma Concentration for Total HuMax-TF (Cojugated and Non-conjugated)[55]

End point description:

End point type	Secondary

End point timeframe:

Part 1: Baseline to end of treatment (Part 1), up to 48 weeks

Notes:

[55] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: hours				
geometric mean (geometric coefficient of variation)				
Cycle 1	36.445 (± 99.474)	14.003 (± 117.534)		
Cycle 1 Day 1	0.747 (± 11.547)	0.893 (± 66.752)		
Cycle 1 Day 8	0.717 (± 0)	0.869 (± 78.568)		
Cycle 1 Day 15	0.727 (± 4.784)	0.896 (± 78.665)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Tmax: Time to Reach the Maximum Plasma Concentration for Total HuMax-TF (Conjugated and Non-conjugated)

End point title	Part 2: Tmax: Time to Reach the Maximum Plasma Concentration for Total HuMax-TF (Conjugated and Non-conjugated)[56]

End point description:

End point type	Secondary

End point timeframe:

Part 2: Baseline to end of trial (Part 2), up to 36 weeks

Notes:

[56] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 2 is displayed for this endpoint.

End point values	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[57]	3[58]		
Units: hours				
geometric mean (geometric coefficient of variation)				
Cycle 1	0.86 (± 73.61)	0.58 (± 22.85)		
Cycle 1 Dose 1	0.86 (± 73.61)	0.58 (± 22.85)		
Cycle 1 Dose 2	165.06 (± 75.01)	106 (± 55.38)		
Cycle 1 Dose 3	71.23 (± 24.35)	80.37 (± 20.24)		

Notes:

[57] - Cycle 1 Dose 2: n = 9
Cycle 1 Dose 3: n = 6
[58] - Cycle 1 Dose 3: n = 2

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Terminal Phase Elimination Half-life (T1/2) for Total HuMax-TF (Cojugated and Non-conjugated)

End point title	Part 1: Terminal Phase Elimination Half-life (T1/2) for Total HuMax-TF (Cojugated and Non-conjugated)[59]

End point description:

End point type	Secondary

End point timeframe:

Part 1: Baseline to end of treatment (Part 1), up to 48 weeks

Notes:

[59] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: hours				
geometric mean (geometric coefficient of variation)	49.56 (± 17.35)	49.34 (± 19.18)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1 and Part 2: Total Clearance (CL) of Total HuMax-TF (Conjugated and Non-conjugated)

End point title	Part 1 and Part 2: Total Clearance (CL) of Total HuMax-TF (Conjugated and Non-conjugated)[60]

End point description:

CL could not be estimated for Part 1 or Part 2 participants due to insufficient samples taken.

End point type	Secondary

End point timeframe:

Part 1 & Part 2: Baseline to end of trial (Part 1 & Part 2), approximately 21 months

Notes:

[60] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: CL could not be calculated, therefore no data is present.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[61]	0[62]	0[63]	0[64]
Units: mL/h/kg				
geometric mean (geometric coefficient of variation)	()	()	()	()

Notes:

[61] - CL could not be estimated.

[62] - CL could not be estimated.

[63] - CL could not be estimated.

[64] - CL could not be estimated.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Trough Concentration (Ctrough) Steady State Plasma Pharmacokinetic for Total HuMax-TF (Conjugated and Non-conjugated)

End point title	Part 1: Trough Concentration (Ctrough) Steady State Plasma Pharmacokinetic for Total HuMax-TF (Conjugated and Non-conjugated)[65]

End point description:

End point type	Secondary

End point timeframe:

Part 1: Baseline to end of treatment, up to 48 weeks

Notes:

[65] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1	150.0 (± 0)	150.0 (± 0)		
Cycle 1 Day 8	1273.1 (± 23.4)	1252.2 (± 53.3)		
Cycle 1 Day 15	1625.1 (± 24.4)	1863.8 (± 46.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1 & Part 2: Apparent Volume of Distribution (Vz) for Total HuMax-TF (Cojugated and Non-conjugated)

End point title	Part 1 & Part 2: Apparent Volume of Distribution (Vz) for Total HuMax-TF (Cojugated and Non-conjugated)[66]

End point description:

Vz/F could not be estimated for Part 1 or Part 2 participants due to insufficient samples taken.

End point type	Secondary

End point timeframe:

Part 1 & Part 2: Baseline to end of trial (Part 1 & Part 2), approximately 21 months

Notes:

[66] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Vz could not be calculated, therefore no data is present.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[67]	0[68]	0[69]	0[70]
Units: mL/kg				
geometric mean (geometric coefficient of variation)	()	()	()	()

Notes:

[67] - Vz/F could not be estimated.

[68] - Vz/F could not be estimated.

[69] - Vz/F could not be estimated.

[70] - Vz/F could not be estimated.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: AUC0-t: Area Under the Plasma Concentration-Time Curve From Time 0 to the Time of Last Quantifiable Concentration for free toxin (MMAE)

End point title	Part 1: AUC0-t: Area Under the Plasma Concentration-Time Curve From Time 0 to the Time of Last Quantifiable Concentration for free toxin (MMAE)[71]

End point description:

End point type	Secondary

End point timeframe:

Part 1 Dose Escalation: Baseline to end of treatment, up to 48 weeks.

Notes:

[71] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	885 (± 27.1)	968 (± 59.7)		

Cycle 1 Day 1	185 (± 48.1)	185 (± 75.3)		
Cycle 1 Day 8	180 (± 14.1)	236 (± 75.5)		
Cycle 1 Day 15	506 (± 25.3)	520 (± 51.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: AUC0-t: Area Under the Plasma Concentration-Time Curve From Time 0 to the Time of Last Quantifiable Concentration for free toxin (MMAE)

End point title	Part 2: AUC0-t: Area Under the Plasma Concentration-Time Curve From Time 0 to the Time of Last Quantifiable Concentration for free toxin (MMAE)[72]

End point description:

9999 has been recorded when there is no data available for the data point. Arms only included 1 participant, no Geometric Coefficient of Variation could be calculated.

9999 has been entered For Arms 'Part 2 Cohort Expansion: Cohort 5 1q3w Ovarian' and 'Part 2 Cohort Expansion: Cohort 6 1q3w Cervical'; as data is only available at Cycle 1 due to changes in dosing schedule. Participants in these arms are only dosed once every 3 weeks (1q3wk).

End point type	Secondary

End point timeframe:

Part 2 Cohort Expansion: Baseline to end of trial, up to 36 weeks.

Notes:

[72] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 2 is displayed for this endpoint.

End point values	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[73]	3[74]		
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	920 (± 74.5)	1049 (± 89.4)		
Cycle 1 Dose 1	439 (± 69.3)	393 (± 100.0)		
Cycle 1 Dose 2	378 (± 121.3)	366 (± 77.9)		
Cycle 1 Dose 3	713 (± 49.9)	494 (± 121.7)		

Notes:

[73] - Cycle 1 Dose 2: n = 9
Cycle 1 Dose 3: n = 6
[74] - Cycle 1 Dose 3: n = 2

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Cmax: Maximum Observed Plasma Concentration for free toxin (MMAE)

End point title	Part 1: Cmax: Maximum Observed Plasma Concentration for free toxin (MMAE)[75]

End point description:

End point type	Secondary

End point timeframe:

Part 1 Dose Escalation: Baseline to end of treatment, up to 48 weeks.

Notes:

[75] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	2.76 (± 23.7)	2.88 (± 52.4)		
Cycle 1 Day 1	1.46 (± 54.7)	1.38 (± 78.4)		
Cycle 1 Day 8	1.18 (± 19.8)	1.54 (± 75.4)		
Cycle 1 Day 15	2.76 (± 23.7)	2.88 (± 52.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Cmax: Maximum Observed Plasma Concentration for free toxin (MMAE)

End point title	Part 2: Cmax: Maximum Observed Plasma Concentration for free toxin (MMAE)[76]

End point description:

End point type	Secondary

End point timeframe:

Part 2 Cohort Expansion: Baseline to end of trial, up to 36 weeks.

Notes:

[76] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 2 is displayed for this endpoint.

End point values	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[77]	3[78]		
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	3.9 (± 97.0)	3.6 (± 101.4)		
Cycle 1 Dose 1	1.9 (± 110.5)	1.5 (± 80.4)		
Cycle 1 Dose 2	2.47 (± 136.4)	2.50 (± 81.1)		
Cycle 1 Dose 3	3.78 (± 81.6)	3.23 (± 125.0)		

Notes:

[77] - Cycle 1 Dose 2: n = 9
Cycle 1 Dose 3: n = 6
[78] - Cycle 1 Dose 3: n = 2

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Tmax: Time to Reach the Maximum Plasma Concentration for free toxin (MMAE)

End point title	Part 1: Tmax: Time to Reach the Maximum Plasma Concentration for free toxin (MMAE)[79]

End point description:

End point type	Secondary

End point timeframe:

Part 1 Dose Escalation: Baseline to end of treatment, up to 48 weeks.

Notes:

[79] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: hours				
geometric mean (geometric coefficient of variation)				
Cycle 1	392.024 (± 3.256)	373.366 (± 6.290)		
Cycle 1 Day 1	44.568 (± 114.567)	32.001 (± 125.788)		
Cycle 1 Day 8	10.354 (± 165.509)	20.837 (± 106.094)		
Cycle 1 Day 15	54.511 (± 20.424)	32.537 (± 63.879)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Tmax: Time to Reach the Maximum Plasma Concentration for free toxin (MMAE)

End point title	Part 2: Tmax: Time to Reach the Maximum Plasma Concentration for free toxin (MMAE)[80]

End point description:

End point type	Secondary

End point timeframe:

Part 2 Cohort Expansion: Baseline to end of trial, up to 36 weeks.

Notes:

[80] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 2 is displayed for this endpoint.

End point values	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[81]	3[82]		
Units: hours				
geometric mean (geometric coefficient of variation)				
Cycle 1	307.05 (± 36.52)	410.61 (± 3.82)		
Cycle 1 Dose 1	160.56 (± 5.66)	162.19 (± 1.71)		
Cycle 1 Dose 2	164.82 (± 56.71)	106.93 (± 55.38)		
Cycle 1 Dose 3	78.37 (± 50.26)	80.37 (± 20.24)		

Notes:

[81] - Cycle 1 Dose 2: n = 9
Cycle 1 Dose 3: n - 6
[82] - Cycle 1 Dose 3: n = 2

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Trough Concentration (Ctrough) Steady State Plasma Pharmacokinetic for free toxin (MMAE)

End point title	Part 1: Trough Concentration (Ctrough) Steady State Plasma Pharmacokinetic for free toxin (MMAE)[83]

End point description:

End point type	Secondary

End point timeframe:

Part 1 Dose Escalation: Baseline to end of treatment, up to 48 weeks.

Notes:

[83] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: pg/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1	12.50 (± 0)	12.50 (± 0)		
Cycle 1 Day 8	853.42 (± 22.93)	1061.28 (± 87.81)		
Cycle 1 Day 15	1013.22 (± 14.47)	1384.29 (± 83.43)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Number of Participants with a Positive Anti-drug antibody (ADA) Immunogenicity Result

End point title	Part 1: Number of Participants with a Positive Anti-drug antibody (ADA) Immunogenicity Result[84]

End point description:

End point type	Secondary

End point timeframe:

Part 1 Dose Escalation: Baseline to end of trial, up to 48 weeks.

Notes:

[84] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Number of Participants with a Positive Anti-drug antibody (ADA) Immunogenicity Result

End point title	Part 2: Number of Participants with a Positive Anti-drug antibody (ADA) Immunogenicity Result[85]

End point description:

End point type	Secondary

End point timeframe:

Part 2 Cohort Expansion: Baseline to end of trial, up to 36 weeks.

Notes:

[85] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 2 is displayed for this endpoint.

End point values	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical	Part 2: Cohort Expansion: Cohort 3 3q4wk - 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 4 3q4wk - 1q3w Cervical
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	3	1	5
Units: Participants	0	0	0	0

End point values	Part 2: Cohort Expansion: Cohort 5 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 6 1q3w Cervical		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	3		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Number of Patients who experienced anti-tumor activity measured by tumor shrinkage

End point title	Part 1: Number of Patients who experienced anti-tumor activity measured by tumor shrinkage[86]

End point description:

End point type	Secondary

End point timeframe:

Part 1 Dose Escalation: Baseline to end of treatment, up to 48 weeks.

Notes:

[86] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: Participants	1	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Anti-tumor Activity Measured by Percentage of Change in Sum of Lesion Measurements

End point title	Part 2: Anti-tumor Activity Measured by Percentage of Change in Sum of Lesion Measurements[87]

End point description:

9999 has been used when there is no data. As the arm only includes 1 participants, there is no Standard Deviation data to enter.

End point type	Secondary

End point timeframe:

Part 2 Cohort Expansion: Baseline to end of trial, up to 36 weeks.

Notes:

[87] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 2 is displayed for this endpoint.

End point values	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical	Part 2: Cohort Expansion: Cohort 3 3q4wk - 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 4 3q4wk - 1q3w Cervical
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	3	1	5
Units: percent				
arithmetic mean (standard deviation)	-17.34 (± 43.388)	32.78 (± 83.933)	-63.27 (± 9999)	0.74 (± 21.877)

End point values	Part 2: Cohort Expansion: Cohort 5 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 6 1q3w Cervical		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	3		
Units: percent				
arithmetic mean (standard deviation)	0 (± 9999)	11.76 (± 27.658)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Response Evaluation based on PSA (Prostate specific antigen [Prostate Cancer]): Percentage of Change from Baseline to End of Study

End point title	Part 1: Response Evaluation based on PSA (Prostate specific antigen [Prostate Cancer]): Percentage of Change from Baseline to End of Study [88]

End point description:

9999 has been recorded when there is no data to enter for a data point. As only 1 participant is included in the data set, there is no Standard Deviation.

End point type	Secondary

End point timeframe:

Part 1 Dose Escalation: Baseline until end of treatment, up to 48 weeks.

Notes:

[88] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	1		
Units: percent				
arithmetic mean (standard deviation)	23.42 (± 61.686)	12.97 (± 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Response Evaluation based on CA125 (Cancer Antigen 125 [Ovarian and Endometrial cancer]): Percentage of Change from Baseline to End of Study

End point title	Part 1: Response Evaluation based on CA125 (Cancer Antigen 125 [Ovarian and Endometrial cancer]): Percentage of Change from Baseline to End of Study [89]

End point description:

9999 has been recorded when there is no data to enter for a data point. Only 1 participant is included in the arm, so no Standard Deviation could be calculated.

End point type	Secondary

End point timeframe:

Part 1 Dose Escalation: Baseline to end of treatment, up to 48 weeks.

Notes:

[89] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[90]	1		
Units: percent				
arithmetic mean (standard deviation)	()	186.21 (± 9999)		

Notes:

[90] - No participants with the indication of Ovarian or Endometrial Cancer had results at the End of Study

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Response Evaluation based on CA125 (Ovarian and Endometrial cancer): Percentage of Change from Baseline to End of Study

End point title	Part 2: Response Evaluation based on CA125 (Ovarian and Endometrial cancer): Percentage of Change from Baseline to End of Study[91]

End point description:

9999 has been recorded when there is no data to recorded for a data point. As only 1 participant was included in the arm, no Standard Deviation could be calculated.

End point type	Secondary

End point timeframe:

Part 2 Cohort Expansion: Baseline to end of trial, up to 36 weeks.

Notes:

[91] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 2 is displayed for this endpoint.

End point values	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical	Part 2: Cohort Expansion: Cohort 3 3q4wk - 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 4 3q4wk - 1q3w Cervical
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	0[92]	1	0[93]
Units: percent				
arithmetic mean (standard deviation)	-31.75 (± 36.235)	()	-32.50 (± 9999)	()

Notes:

[92] - CA125 was assessed in patients with ovarian or endometrial cancer only.

[93] - CA125 was assessed in patients with ovarian or endometrial cancer only.

End point values	Part 2: Cohort Expansion: Cohort 5 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 6 1q3w Cervical		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[94]	0[95]		
Units: percent				
arithmetic mean (standard deviation)	()	()		

Notes:

[94] - No participants with the indication of Ovarian Cancer had results at End of Study.

[95] - CA125 was assessed in patients with ovarian or endometrial cancer only.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Best Overall Response (OR)

End point title	Part 1: Best Overall Response (OR)[96]

End point description:

Best OR (by investigators assessment) was the best response recorded from the start of the treatment until disease progression or death. Complete response: the disappearance of all target lesions. Any pathological lymph nodes must have reduction in short axis to < 10 mm. Based on non-target lesions, complete response was defined as disappearance of all non-target lesions and normalization of tumor marker level. All lymph nodes must be non-pathological in size (< 10 mm short axis).

Partial response (PR): ≥ 30% decrease in the sum of the longest diameter (LD) of target lesions, taking as reference the baseline sum of LDs.

Stable disease: neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease (PD), taking as reference the smallest sum of LDs while in trial. Based on non-target lesions, stable disease was defined as persistence of 1 or more non-target lesion(s) or/and maintenance of tumor marker level above the normal limits.

End point type	Secondary

End point timeframe:

Part 1 Dose Escalation: Baseline to end of treatment (Part 1), up to 48 weeks

Notes:

[96] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: Participants				
Complete Response	0	0		
Partial Response	0	1		
Stable Disease	2	3		
Progressive Disease	1	1		
Not Evaluable	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Best Overall Response (OR)

End point title	Part 2: Best Overall Response (OR)[97]

End point description:

Best OR (by investigators assessment) was the best response recorded from the start of the treatment until disease progression or death. Complete response: the disappearance of all target lesions. Any pathological lymph nodes must have reduction in short axis to < 10 mm. Based on non-target lesions, complete response was defined as disappearance of all non-target lesions and normalization of tumor marker level. All lymph nodes must be non-pathological in size (< 10 mm short axis).

Partial response (PR): ≥ 30% decrease in the sum of the longest diameter (LD) of target lesions, taking as reference the baseline sum of LDs.

Stable Disease: neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease (PD), taking as reference the smallest sum of LDs while in trial. Based on non-target lesions, stable disease was defined as persistence of 1 or more non-target lesion(s) or/and maintenance of tumor marker level above the normal limits.

End point type	Secondary

End point timeframe:

Part 2 Cohort Expansion: Baseline to end of trial (Part 2), up to 36 weeks

Notes:

[97] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No formal statistical tests were performed for this trial

End point values	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical	Part 2: Cohort Expansion: Cohort 3 3q4wk - 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 4 3q4wk - 1q3w Cervical
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	3	1	5
Units: Participants				
Complete Response	0	0	0	0
Partial Response	3	1	1	2
Stable Disease	3	0	0	2
Progressive Disease	2	2	0	1
Not Evaluable	3	0	0	0

End point values	Part 2: Cohort Expansion: Cohort 5 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 6 1q3w Cervical		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	3		
Units: Participants				
Complete Response	0	0		
Partial Response	0	0		
Stable Disease	0	2		
Progressive Disease	1	1		
Not Evaluable	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Number of Participants who experienced Disease Control

End point title	Part 1: Number of Participants who experienced Disease Control [98]

End point description:

End point type	Secondary

End point timeframe:

Part 1 Dose Escalation: 6, 12, 24 and 36 weeks post first dose.

Notes:

[98] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: Participants				
6 Weeks	2	3		
12 Weeks	0	0		
24 Weeks	0	0		
36 Weeks	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Number of Participants who experienced Disease Control

End point title	Part 2: Number of Participants who experienced Disease Control[99]

End point description:

End point type	Secondary

End point timeframe:

Part 2 Cohort Expansion: 6, 12, 24 and 36 weeks post first dose.

Notes:

[99] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 2 is displayed for this endpoint.

End point values	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical	Part 2: Cohort Expansion: Cohort 3 3q4wk - 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 4 3q4wk - 1q3w Cervical
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	3	1	5
Units: Participants				
6 Weeks	6	1	1	4
12 Weeks	2	1	1	2
24 Weeks	0	0	0	1
36 Weeks	0	0	0	0

End point values	Part 2: Cohort Expansion: Cohort 5 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 6 1q3w Cervical		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	3		

Units: Participants				
6 Weeks	0	2		
12 Weeks	0	1		
24 Weeks	0	0		
36 Weeks	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Proportion of Patients with Progression Free Survival

End point title	Part 1: Proportion of Patients with Progression Free Survival [100]

End point description:

Based on target lesions, progressive disease was defined as ≥ 20% (and ≥ 5 m m) increase in the sum of the LDs of target lesions, taking as reference the smallest sum of the target LDs recorded while in trial or the appearance of 1 or more new lesions. Based on non-target lesions, progressive disease was defined as the appearance of 1 or more new lesions and/or unequivocal progression of existing non-target lesions. The proportion of patients with PFS will be summarized using Kaplan-Meier estimates.

End point type	Secondary

End point timeframe:

Part 1 Dose Escalation: 12, 24, 36, 48 and 60 Weeks Post first dose.

Notes:

[100] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: percentage of participants				
number (not applicable)				
12 Weeks	50	67		
24 Weeks	0	67		
36 Weeks	0	67		
48 Weeks	0	67		
60 Weeks	0	67		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Proportion of Patients with Progression Free Survival

End point title	Part 2: Proportion of Patients with Progression Free Survival[101]

End point description:

Based on target lesions, progressive disease was defined as ≥ 20% (and ≥ 5 m m) increase in the sum of the LDs of target lesions, taking as reference the smallest sum of the target LDs recorded while in trial or the appearance of 1 or more new lesions. Based on non-target lesions, progressive disease was defined as the appearance of 1 or more new lesions and/or unequivocal progression of existing non-target lesions. The proportion of patients with PFS will be summarized using Kaplan-Meier estimates.

End point type	Secondary

End point timeframe:

Part 2 Cohort Expansion: 12, 24 and 36 weeks post first dose.

Notes:

[101] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 2 is displayed for this endpoint.

End point values	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical	Part 2: Cohort Expansion: Cohort 3 3q4wk - 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 4 3q4wk - 1q3w Cervical
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	3	1	5
Units: percentage of participants				
number (not applicable)				
12 Weeks	39	33	100	60
24 Weeks	39	33	0	20
36 Weeks	39	33	0	20

End point values	Part 2: Cohort Expansion: Cohort 5 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 6 1q3w Cervical		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	3		
Units: percentage of participants				
number (not applicable)				
12 Weeks	0	33		
24 Weeks	0	0		
36 Weeks	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Duration of Response

End point title	Part 1: Duration of Response[102]

End point description:

Duration of response was defined as as the number of days from the first documentation of objective tumor response (complete response [CR] or partial response [PR]) to the date of first progressive disease (PD) or death.

Duration of Response could not be estimated as participants with a confirmed response were discontinued due to toxicity or other reason different from PD or death.

End point type	Secondary

End point timeframe:

Part 1 Dose Escalation: Baseline to end of treatment, up to 48 weeks.

Notes:

[102] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 1 is displayed for this endpoint.

End point values	Part 1: Dose Escalation: Cohort 1 3q4wk 0.9 mg/kg	Part 1: Dose Escalation: Cohort 2 3q4wk 1.2 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[103]	0[104]		
Units: Weeks				
median (confidence interval 95%)	(to)	(to)		

Notes:

[103] - Duration of response could not be calculated due to insufficient number of participants.

[104] - 1 participant was responder but DOR was censored, therefore duration of response was not calculated

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Duration of Response

End point title	Part 2: Duration of Response[105]

End point description:

Duration of response was defined as as the number of days from the first documentation of objective tumor response (CR or PR) to the date of first PD or death.

Duration of Response could not be estimated as patients with a confirmed response were discontinued due to toxicity or other reason different from PD or death.

End point type	Secondary

End point timeframe:

Part 2 Cohort Expansion: Baseline to end of trial, up to 36 weeks.

Notes:

[105] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Study was conducted in 2 parts; Part 1 Dose Escalation and Part 2 Cohort Expansion. Only data for Part 2 is displayed for this endpoint.

End point values	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical	Part 2: Cohort Expansion: Cohort 3 3q4wk - 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 4 3q4wk - 1q3w Cervical
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[106]	0[107]	0[108]	0[109]
Units: Weeks				
number (not applicable)				

Notes:

[106] - Duration of response could not be calculated as participants discontinued.

[107] - Duration of response could not be calculated as participants discontinued.

[108] - Duration of response could not be calculated as participants discontinued.

[109] - Duration of response could not be calculated as participants discontinued.

End point values	Part 2: Cohort Expansion: Cohort 5 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 6 1q3w Cervical		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[110]	0[111]		
Units: Weeks				
number (not applicable)				

Notes:

[110] - Duration of response could not be calculated as participants discontinued.

[111] - Duration of response could not be calculated as participants discontinued.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline to End of Trial (Part 1 &2), approximately 21 Months.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Part 1: Dose Escalation: Cohort 1 0.9mg/kg

Reporting group description:

Tisotumab vedotin 0.9 mg/kg was administered as an intravenous infusion, over a minimum of 30 minutes, 3 times every 4 weeks (3q4wk).

Reporting group title	Part 1: Dose Escalation: Cohort 2 1.2 mg/kg

Reporting group description:

Tisotumab vedotin 1.2 mg/kg was administered as an intravenous infusion, over a minimum of 30 minutes, 3 times every 4 weeks (3q4wk).

Reporting group title	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian

Reporting group description:

Participants with the indication of ovarian cancer, received Tisotumab vedotin 1.2 mg/kg (the recommended dose for phase II trials [RP2D] from the Dose Escalation part), administered as an intravenous infusion, over a minimum of 30 minutes 3 times every 4 weeks (3q4wk).

Reporting group title	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical

Reporting group description:

Participants with the indication of cervical cancer, received Tisotumab vedotin 1.2 mg/kg (RP2D from the Dose Escalation part), administered as an intravenous infusion, over a minimum of 30 minutes 3 times every 4 weeks (3q4wk).

Reporting group title	Part 2: Cohort Expansion: Cohort 3 3q4wk - 1q3w Ovarian

Reporting group description:

Participants with the indication of ovarian cancer, received Tisotumab vedotin 1.2 mg/kg (RP2D from the Dose Escalation part), administered as an intravenous infusion, over a minimum of 30 minutes 3 times every 4 weeks (3q4wk). Due to severe ocular toxicity, participants continued to receive Tisotumab vedotin at 2.0 mg/kg, administered as an intravenous infusion, over a minimum of 30 minutes, once every 3 weeks (1q3w).

Reporting group title	Part 2: Cohort Expansion: Cohort 4 3q4wk - 1q3w Cervical

Reporting group description:

Participants with the indication of cervical cancer, received Tisotumab vedotin 1.2 mg/kg (RP2D from the Dose Escalation part), administered as an intravenous infusion, over a minimum of 30 minutes 3 times every 4 weeks (3q4wk). Due to severe ocular toxicity, participants continued to receive Tisotumab vedotin at 2.0 mg/kg, administered as an intravenous infusion, over a minimum of 30 minutes, once every 3 weeks (1q3w).

Reporting group title	Part 2: Cohort Expansion: Cohort 5 1q3w Ovarian

Reporting group description:

Participants with the indication of ovarian cancer, received Tisotumab vedotin 2.0 mg/kg, administered as an intravenous infusion, over a minimum of 30 minutes, once every 3 weeks (1q3w).

Reporting group title	Part 2: Cohort Expansion: Cohort 6 1q3w Cervical

Reporting group description:

Participants with the indication of cervical cancer, received Tisotumab vedotin 2.0 mg/kg, administered as an intravenous infusion, over a minimum of 30 minutes, once every 3 weeks (1q3w).

Serious adverse events	Part 1: Dose Escalation: Cohort 1 0.9mg/kg	Part 1: Dose Escalation: Cohort 2 1.2 mg/kg	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	2 / 6 (33.33%)	9 / 11 (81.82%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	1
Cardiac disorders			
Atrial flutter			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Disease progression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Symblepharon			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	4 / 11 (36.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Nauea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colonic pseudo-obstruction			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			

subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	3 / 11 (27.27%)
occurrences causally related to treatment / all	1 / 1	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical	Part 2: Cohort Expansion: Cohort 3 3q4wk - 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 4 3q4wk - 1q3w Cervical
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)	0 / 1 (0.00%)	2 / 5 (40.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
Atrial flutter			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			

General physical health deterioration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disease progression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Symblepharon			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Nauea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colonic pseudo-obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Small intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			

Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 2: Cohort Expansion: Cohort 5 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 6 1q3w Cervical	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Atrial flutter			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease progression			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Symblepharon			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Nauea			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colonic pseudo-obstruction			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			

subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Part 1: Dose Escalation: Cohort 1 0.9mg/kg	Part 1: Dose Escalation: Cohort 2 1.2 mg/kg	Part 2: Cohort Expansion: Cohort 1 3q4wk Ovarian
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	6 / 6 (100.00%)	11 / 11 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Hypotension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	3
Lymphoedema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 3 (66.67%)	2 / 6 (33.33%)	6 / 11 (54.55%)
occurrences (all)	2	2	8
Chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Pain			
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Pyrexia			

subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Oedema peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Female genital tract fistula			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	3 / 3 (100.00%)	5 / 6 (83.33%)	7 / 11 (63.64%)
occurrences (all)	4	5	8
Nasal congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	2 / 11 (18.18%)
occurrences (all)	1	0	2
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	3
Dysphonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Laryngeal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Nasal dryness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Pulmonary haemorrhage			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Sinus congestion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	3
Weight decreased			
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	2 / 11 (18.18%)
occurrences (all)	1	1	2
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	3
Vital dye staining cornea present			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
International normalised ratio increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Lymphocyte count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Urine output increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Radiation proctitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Neuropathy peripheral			
subjects affected / exposed	0 / 3 (0.00%)	4 / 6 (66.67%)	1 / 11 (9.09%)
occurrences (all)	0	4	1
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Headache			

subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Polyneuropathy			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Dizziness			
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	2 / 11 (18.18%)
occurrences (all)	1	0	4
Febrile neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	7
Blepharitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Eye pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	2
Keratitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Meibomianitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			

subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Symblepharon			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Punctate keratitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	2
Episcleritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Keratopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Ocular hyperaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Ulcerative keratitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	3 / 11 (27.27%)
occurrences (all)	0	3	4
Constipation			
subjects affected / exposed	0 / 3 (0.00%)	4 / 6 (66.67%)	5 / 11 (45.45%)
occurrences (all)	0	5	5
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	3 / 6 (50.00%)	4 / 11 (36.36%)
occurrences (all)	0	3	4
Nausea			
subjects affected / exposed	2 / 3 (66.67%)	2 / 6 (33.33%)	5 / 11 (45.45%)
occurrences (all)	2	2	6
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	4 / 11 (36.36%)
occurrences (all)	0	0	6

Abdominal discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Abdominal pain lower			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Haematochezia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Lip ulceration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Melaena			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Mouth ulceration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Rectal discharge			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Tongue blistering			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0

Oedema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	5 / 11 (45.45%)
occurrences (all)	0	1	5
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Rash			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Rash maculo-papular			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Dry skin			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	0 / 11 (0.00%)
occurrences (all)	0	4	0
Acute kidney injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Cystitis noninfective			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	2 / 11 (18.18%)
occurrences (all)	0	1	3
Myalgia			
subjects affected / exposed	1 / 3 (33.33%)	3 / 6 (50.00%)	3 / 11 (27.27%)
occurrences (all)	1	3	3
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	1 / 11 (9.09%)
occurrences (all)	0	3	1
Muscle spasms			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Bone pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	2 / 3 (66.67%)	6 / 6 (100.00%)	5 / 11 (45.45%)
occurrences (all)	2	12	6
Urinary tract infection			

subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	2
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Cystitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Rash pustular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Escherichia vaginitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Oral herpes			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Pneumonia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Tonsillitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			

Decreased appetite			
subjects affected / exposed	2 / 3 (66.67%)	3 / 6 (50.00%)	5 / 11 (45.45%)
occurrences (all)	2	4	5
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	2 / 11 (18.18%)
occurrences (all)	0	2	3
Hypomagnesaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	2 / 11 (18.18%)
occurrences (all)	0	1	2
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Cell death			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Hypocalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	2
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Hyperlipidaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Part 2: Cohort Expansion: Cohort 2 3q4wk Cervical	Part 2: Cohort Expansion: Cohort 3 3q4wk - 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 4 3q4wk - 1q3w Cervical
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	1 / 1 (100.00%)	5 / 5 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Lymphoedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 3 (33.33%)	1 / 1 (100.00%)	4 / 5 (80.00%)
occurrences (all)	1	1	6
Chest pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	2	0	1
Malaise			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Female genital tract fistula			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1

Vaginal haemorrhage			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	1 / 3 (33.33%)	1 / 1 (100.00%)	3 / 5 (60.00%)
occurrences (all)	1	1	3
Nasal congestion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 1 (100.00%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dysphonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Laryngeal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Nasal dryness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pulmonary haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Rhinorrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Sinus congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			

Depression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Weight decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vital dye staining cornea present			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
International normalised ratio increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Neutrophil count decreased			

subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Platelet count decreased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Urine output increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Radiation proctitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Neuropathy peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	2
Headache			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
Polyneuropathy			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	2	0	2
Febrile neutropenia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	3 / 5 (60.00%)
occurrences (all)	0	0	3
Blepharitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Eye pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Keratitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	2 / 5 (40.00%)
occurrences (all)	0	0	4
Meibomianitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Lacrimation increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Symblepharon			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Punctate keratitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Episcleritis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Keratopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Ocular hyperaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Ulcerative keratitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	4 / 5 (80.00%)
occurrences (all)	1	0	6
Constipation			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	2 / 5 (40.00%)
occurrences (all)	1	0	2
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 1 (100.00%)	3 / 5 (60.00%)
occurrences (all)	0	1	4
Nausea			
subjects affected / exposed	1 / 3 (33.33%)	1 / 1 (100.00%)	1 / 5 (20.00%)
occurrences (all)	1	1	1
Vomiting			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
Abdominal discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Abdominal pain upper			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	2
Abdominal pain lower			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1

Dry mouth			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Lip ulceration			
subjects affected / exposed	0 / 3 (0.00%)	1 / 1 (100.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Melaena			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Mouth ulceration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Rectal discharge			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Rectal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tongue blistering			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Oedema			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 1 (100.00%)	3 / 5 (60.00%)
occurrences (all)	1	1	3
Pruritus			

subjects affected / exposed	1 / 3 (33.33%)	1 / 1 (100.00%)	1 / 5 (20.00%)
occurrences (all)	1	1	1
Rash			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	2
Rash maculo-papular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Acute kidney injury			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Cystitis noninfective			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Pollakiuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Urinary incontinence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Muscle spasms			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	2 / 5 (40.00%)
occurrences (all)	0	0	2
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	2 / 5 (40.00%)
occurrences (all)	0	0	2
Bone pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	3 / 5 (60.00%)
occurrences (all)	0	0	6
Urinary tract infection			
subjects affected / exposed	1 / 3 (33.33%)	1 / 1 (100.00%)	1 / 5 (20.00%)
occurrences (all)	1	1	1
Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	2
Upper respiratory tract infection			

subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Rash pustular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Escherichia vaginitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	1
Oral herpes			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 3 (33.33%)	1 / 1 (100.00%)	1 / 5 (20.00%)
occurrences (all)	1	1	1
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	3 / 5 (60.00%)
occurrences (all)	0	0	3

Hypomagnesaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	2
Cell death			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Hypophosphataemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hyperlipidaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part 2: Cohort Expansion: Cohort 5 1q3w Ovarian	Part 2: Cohort Expansion: Cohort 6 1q3w Cervical	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)	3 / 3 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Hypertension			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	

Hypotension			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Lymphoedema			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 1 (0.00%)	2 / 3 (66.67%)	
occurrences (all)	0	3	
Chest pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Malaise			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Pyrexia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Oedema peripheral			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Female genital tract fistula			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Vaginal haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			

subjects affected / exposed	0 / 1 (0.00%)	2 / 3 (66.67%)	
occurrences (all)	0	5	
Nasal congestion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Cough			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Dyspnoea			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Dysphonia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Laryngeal haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Nasal dryness			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Pulmonary haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Rhinorrhoea			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Sinus congestion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Insomnia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	

Anxiety			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Weight decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Vital dye staining cornea present			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
International normalised ratio increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Lymphocyte count decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Neutrophil count decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Platelet count decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Urine output increased			

subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
White blood cell count decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Radiation proctitis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Neuropathy peripheral			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Polyneuropathy			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Dizziness			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	2	
Febrile neutropenia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	

Neutropenia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Blepharitis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Eye pain			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Keratitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Meibomianitis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Lacrimation increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Symblepharon			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Punctate keratitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Episcleritis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Keratopathy			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Ocular hyperaemia			

subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Ulcerative keratitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 1 (0.00%)	2 / 3 (66.67%)	
occurrences (all)	0	2	
Constipation			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Abdominal pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Nausea			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Vomiting			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Abdominal discomfort			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Abdominal pain upper			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Abdominal pain lower			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Dry mouth			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Haematochezia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	

Lip ulceration			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Melaena			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Mouth ulceration			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Rectal discharge			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Rectal haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Dyspepsia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Tongue blistering			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Oedema			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 1 (0.00%)	2 / 3 (66.67%)	
occurrences (all)	0	2	
Pruritus			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Rash			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Rash maculo-papular			

subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Dry skin			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Erythema			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 1 (0.00%)	2 / 3 (66.67%)	
occurrences (all)	0	4	
Acute kidney injury			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Cystitis noninfective			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Dysuria			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Pollakiuria			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Urinary incontinence			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	2	
Myalgia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Arthralgia			

subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Muscle spasms			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Pain in extremity			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Bone pain			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Flank pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Muscular weakness			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	2	
Infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Cystitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Rash pustular			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	

Rhinitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Escherichia vaginitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Influenza			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Oral herpes			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Pneumonia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Tonsillitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Hypokalaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Hypomagnesaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Hyponatraemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Cell death			

subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Hypocalcaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Hypophosphataemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Dehydration			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Hyperlipidaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 July 2016	The main purpose of Protocol Amendment 1 was to add a Cohort Expansion part to the existing Dose Escalation part of the trial. The Cohort Expansion part of the trial was a phase II trial designed to gather additional safety, tolerability, PK and anti-tumor activity data by exposing patients to the R2PD established in the Dose Escalation part. For the Cohort Expansion part, additional phase II sites were planned to be opened in the ongoing countries (Denmark, the UK and the USA) and in Hungary and Belgium. Other main changes included the following; the international nonproprietary name (INN)/chemical name for HuMax-TF-ADC, tisotumab vedotin was added to the protocol as appropriate. Updated information from clinical experience with tisotumab vedotin in the GEN701 trial and the Dose Escalation part of GEN702 was added to the protocol. Addition of mitigation plan for ocular events. Events of conjunctivitis were not included in the Investigator's Brochure or the Subject ICF for tisotumab vedotin at that time. The protocol was updated to ensure that investigators and patients were informed about the event, and the risk was sufficiently mitigated in the trial going forward. Exclusion criterion #9 was modified to include specifications on blood transfusion and/or erythropoietin use. A 40-day washout period combined with a requirement for no residual check-point inhibitor related symptoms of autoimmune toxicity was added to the protocol. This was based on input provided by investigators and literature review evaluated to accommodate both feasibility of inclusion of patients in the trial as well as patient safety. For the Cohort Expansion part of the trial, the DMC would not hold preplanned meetings but would convene in the event of any safety signals.
27 October 2016	Additional information indicating a need for further risk mitigation activities for events of conjunctivitis was reported to the sponsor. The sponsor, in collaboration with external ophthalmologists, evaluated the need for additional risk mitigation activities. The main purpose of Protocol Amendment 2 was to modify the evaluation and mitigation plan for ocular events, as follows: 1) Baseline ophthalmological assessment as well as ongoing ophthalmological assessment of all patients. 2) Exclusion criteria added concerning patients with active ocular surface disease as well as patients with a medical history of cicatricial conjunctivitis. 3) All patients with ocular symptoms had to undergo prompt ophthalmological assessment. 4) More elaborated criteria for holding dose, reducing dose and treatment withdrawal. 5) Optional treatment guidance for ophthalmological treatment of events of conjunctivitis included for information to the treating ophthalmologist. The Investigator's Brochure and the ICF were updated accordingly. The above-mentioned activities had been discussed and agreed with the DMC for both the GEN701 and GEN702 trials. The new information was not considered to change the overall benefit-risk profile of tisotumab vedotin. Also in Protocol Amendment 2, some inclusion and exclusion criteria were reworded for clarification and/or to adapt to current experience or standard practice.
22 December 2016	This was an urgent safety amendment. One CTCAE grade 3 event of conjunctivitis had already been reported in the GEN702 trial. Following the cut-off date of 31 May 2016, three additional CTCAE grade 3 events of conjunctivitis and one CTCAE grade 4 event of keratitis had been reported with tisotumab vedotin. The purpose of Protocol Amendment 3 was to update this information in the protocol and to modify the dose modification and mitigation plan for ocular events accordingly, including mandatory preventive eye therapy. In addition, reduced dose could be administered in accordance with the added mitigation strategies or at the discretion of the treating physician, and after consultation and agreement by the sponsor Medical Officer.

06 July 2017	This was an urgent safety amendment. The DMC and the Genmab Safety Committee assessed the safety profile observed to date and agreed that patients should not continue treatment at the 1.2 mg/kg 3q4w dose/schedule and supported the following change in dose: the treatment schedule consisting of 2.0 mg/kg dose 1q3w determined from GEN701, which had demonstrated a favorable benefit risk assessment for patients with advanced/metastatic tumors. Additional measurements were also implemented to the mitigation plan for ocular AEs, and a requirement of urgent reporting of non-serious grade 2 ocular events was added. As a consequence of this Protocol Amendment 4, the patient and the investigator had to review continued participation in the GEN702 trial together. If the patient decided to continue all future administrations, the patient would be dosed at 2.0 mg/kg 1q3w, regardless of the prior dose(s) administered. The next dose of tisotumab vedotin could not be administered until at least 21 days had elapsed since the last administration. The sites were also provided with specific instructions for operational handling of switching patients from the 3q4w to the 1q3w dosing scheme. The patients had to sign a new ICF.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported