Clinical trial results:
A multi-center, open-label trial investigating the efficacy and safety of continued treatment with tisotumab vedotin in patients with solid tumors known to express tissue factor

Summary

EudraCT number	2016-004743-37
Trial protocol	BE GB SE HU DK
Global end of trial date	10 January 2019

Results information

Result version number	v1 (current)
This version publication date	14 April 2021
First version publication date	14 April 2021

Trial information

Trial identification

Sponsor protocol code	GCT1015-03

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03245736
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Genmab A/S
Sponsor organisation address	Kalvebod Brygge 43, Copenhagen V, Denmark, DK-1560
Public contact	Clinical Trial Information, Genmab A/S, +45 70202728, clinicaltrials@genmab.com
Scientific contact	Clinical Trial Information, Genmab A/S, +45 70202728, 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	10 January 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 January 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To collect long-term safety data from participants with solid tumors who have been treated with tisotumab vedotin and completed any base trial (i.e., GEN701 - 2013-001074-15 or GEN702 - 2015-001120-29)

Protection of trial subjects:

This trial was conducted in accordance with the International Council for Harmonisation (ICH) Guideline for Good Clinical Practice (GCP) E6 (R2); the United States of America (USA) Food and Drug Administration (FDA) Code of Federal Regulations (CFR) (21 CFR § 50, 56, 312), the Declaration of Helsinki (Fortaleza 2013), and all applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 August 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 1
Country: Number of subjects enrolled	United Kingdom: 4
Worldwide total number of subjects	5
EEA total number of subjects	4

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)	5
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All participants entered the trial following completion of other tisotumab vedotin trials such as GEN701 and GEN702. A total of 5 participants took part in the trial at 3 sites in the United Kingdom and 1 site in the United States from 23 August 2017 to 10 January 2019.

Pre-assignment

Screening details:

Six participants were screened, 5 of which were enrolled.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Tisotumab Vedotin

Arm description:

Tisotumab vedotin was administered as an intravenous (IV) infusion on Day 1 of each 21-day cycle (once every 3 weeks). The trial ran until the investigator determined that the participant was no longer benefiting from treatment (ie, disease progression or unacceptable toxicity had occurred), the trial was terminated by the sponsor, or the participant withdrew consent. Each participant received the same dose that they were exposed to in the previous base trial.

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 injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received 2.0 mg/kg or if dose reduced, the same dose as in base trial by intravenous infusion, over a minimum of 30 minutes.

Number of subjects in period 1	Tisotumab Vedotin
Started	5
Completed	0
Not completed	5
Adverse event, non-fatal	1
Progressive Disease	4

Baseline characteristics

Reporting groups	
Reporting group title	Tisotumab Vedotin

Reporting group description:

Tisotumab vedotin was administered as an intravenous (IV) infusion on Day 1 of each 21-day cycle (once every 3 weeks). The trial ran until the investigator determined that the participant was no longer benefiting from treatment (ie, disease progression or unacceptable toxicity had occurred), the trial was terminated by the sponsor, or the participant withdrew consent. Each participant received the same dose that they were exposed to in the previous base trial.

Reporting group values	Tisotumab Vedotin	Total	
Number of subjects	5	5	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	5	5	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	5	5	
Male	0	0	
Race Units: Subjects			
White	5	5	

End points

End points reporting groups

Reporting group title	Tisotumab Vedotin

Reporting group description:

Tisotumab vedotin was administered as an intravenous (IV) infusion on Day 1 of each 21-day cycle (once every 3 weeks). The trial ran until the investigator determined that the participant was no longer benefiting from treatment (ie, disease progression or unacceptable toxicity had occurred), the trial was terminated by the sponsor, or the participant withdrew consent. Each participant received the same dose that they were exposed to in the previous base trial.

Primary: Number of Participants Who Experienced a Treatment Emergent Adverse Event (TEAE)

End point title	Number of Participants Who Experienced a Treatment Emergent Adverse Event (TEAE)[1]

End point description:

An adverse event (AE) is any untoward medical occurrence in a participant or clinical trial participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Treatment emergent adverse event (TEAE) is an AE occurring on or after the first dose of study medication or worsening during treatment period.

End point type	Primary

End point timeframe:

Day 1 to Week 24 plus 30 days

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: Given the low expected number of participants, no formal statistical analyses were planned.

End point values	Tisotumab Vedotin			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Participants	5			

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate

End point title	Objective Response Rate

End point description:

Objective Response was investigator-assessed based on the Response Evaluation Criteria In Solid Tumors version 1.1 [RECIST 1.1] criteria. The best overall response was reported for each participant.

End point type	Secondary

End point timeframe:

Day 1 to Week 24 plus 30 days

End point values	Tisotumab Vedotin			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Participants				
Complete Response	0			
Partial Response	2			
Stable Disease	2			
Progressive Disease	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Increased Cancer Antigen (CA 125) Levels

End point title	Number of Participants with Increased Cancer Antigen (CA 125) Levels

End point description:

The number of participants with ovarian cancer whose levels of CA125 Antigen had increased since the end of the base trial are presented.

End point type	Secondary

End point timeframe:

Day 1 to Week 24 plus 30 days

End point values	Tisotumab Vedotin			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Participants	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Increased Prostate Specific Antigen (PSA)

End point title	Number of Participants with Increased Prostate Specific Antigen (PSA)

End point description:

The number of participants with prostate cancer whose levels of PSA had increased since the end of the base trial are presented.

End point type	Secondary

End point timeframe:

Day 1 to Week 24 plus 30 days

End point values	Tisotumab Vedotin			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: Participants				

Notes:

[2] - No participants with prostate cancer participated in this trial.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Day 1 to Week 24 plus 30 days	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups	
Reporting group title	Overall

Reporting group description: -

Serious adverse events	Overall		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 5 (20.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Peripheral sensorimotor neuropathy			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Overall		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)		
Vascular disorders			
Venous thrombosis limb			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Thrombophlebitis superficial			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Nervous system disorders			

Neuropathy peripheral subjects affected / exposed occurrences (all) Balance disorder subjects affected / exposed occurrences (all)	4 / 5 (80.00%) 5 1 / 5 (20.00%) 1		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 3		
Blood and lymphatic system disorders Lymphopenia subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Eye disorders Retinal exudates subjects affected / exposed occurrences (all) Ocular toxicity subjects affected / exposed occurrences (all) Corneal thinning subjects affected / exposed occurrences (all) Punctate keratitis subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1 1 / 5 (20.00%) 1 1 / 5 (20.00%) 1 1 / 5 (20.00%) 1		
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)	2 / 5 (40.00%) 2		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 2		
Infections and infestations			

Localised infection subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all)	 1 / 5 (20.00%) 1 1 / 5 (20.00%) 1		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	 2 / 5 (40.00%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 December 2016	The purpose of this protocol amendment was to modify the dose modification and the mitigation plan for ocular events accordingly.
27 July 2017	The purpose for this amendment was to align the treatment schedule with one of the base trials, and implement improved mitigation plan for ocular AE and reporting requirement.
30 November 2017	The protocol was amended to align with one of the base trials updated inclusion and exclusion criteria, permitted concomitant medications and AEs including medication errors, overdose and pregnancies reporting requirement.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported