Clinical trial results:
Dose-escalation, PK and safety study with single agent CetuGEXTM in patients with locally advanced and/or metastatic cancer.

Summary

EudraCT number	2010-019552-50
Trial protocol	DE
Global end of trial date	14 November 2013

Results information

Result version number	v1 (current)
This version publication date	25 April 2019
First version publication date	25 April 2019

Trial information

Trial identification

Sponsor protocol code	GEXMab52101

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01222637
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Glycotope GmbH
Sponsor organisation address	Robert-Roessle-Str. 10, Berlin, Germany, 13125
Public contact	Dr. Alfredo Zurlo, Glycotope GmbH, 030 94892600, alfredo.zurlo@glycotope.com
Scientific contact	Dr. Alfredo Zurlo, Glycotope GmbH, 030 94892600, alfredo.zurlo@glycotope.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	16 March 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 November 2013
Global end of trial reached?	Yes
Global end of trial date	14 November 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

•To evaluate the safety and tolerability profile of CetuGEXTM at various dose levels •To define the recommended phase II dose and regimen

Protection of trial subjects:

The safety data during the study were monitored on a continued basis by an Independent Drug Safety Monitoring Board (DSMB) comprising of 3 experienced physicians. In general, the DSMB provided recommendations if the study could continue as planned in the study protocol, if changes were needed from a safety point of view, or if the maximum tolerated dose (MTD) was reached.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 August 2010
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	Germany: 26
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	Switzerland: 9
Worldwide total number of subjects	41
EEA total number of subjects	32

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)	27
From 65 to 84 years	14

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Date of first enrollment: 25 Aug 2010
Date of last completed: 14 Nov 2013

Pre-assignment

Screening details:

Male or female patients equal or greater 18 years of age with a histologically confirmed locally advanced and/or metastatic solid organ tumor. Patients enrolled in Germany were required to have a positive EGFR overexpression status. Patients must have experienced a failure or non-availability of standard therapy.

Period 1

Period 1 title	Intent-to-treat (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

no blinding

Arms

Arm title	CetuGEX

Arm description:

no other arm

Arm type	Experimental
Investigational medicinal product name	CetuGEX
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Weekly doses of 12 mg, 60 mg, 120 mg, 240 mg, 480 mg, 720 mg, 990 mg, or 1370 mg CetuGEX™ or dosing every 2 weeks of 990 mg CetuGEX™ administered by an intravenous Infusion.

Number of subjects in period 1	CetuGEX
Started	41
Completed	41

Baseline characteristics

Reporting groups	
Reporting group title	Intent-to-treat

Reporting group description: -

Reporting group values	Intent-to-treat	Total	
Number of subjects	41	41	
Age categorical Units: Subjects			
Adults >= 18 years	41	41	
Age continuous			
Adults >= 18 years			
Units: years arithmetic mean standard deviation	 59.8 ± 10.53	 -	
Gender categorical Units: Subjects			
Female	12	12	
Male	29	29	

End points

End points reporting groups

Reporting group title	CetuGEX
Reporting group description: no other arm	

Primary: safety profile adverse event

End point title	safety profile adverse event[1]
End point description:	
End point type	Primary
End point timeframe: All adverse events occurring after the patient entered the study until 28+2 days following the last infusion have been reported.	

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: The number and percentage of patients with treatment-emergent adverse events (TEAEs) were summarized for each cohort and in total for each dosing scheme by system organ class (SOC) and preferred term (PT).

End point values	CetuGEX			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: numbers	41			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics

End point title	Pharmacokinetics
End point description:	
End point type	Secondary
End point timeframe: 2 Treatment Cycles	

End point values	CetuGEX			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: milligram(s)				
number (not applicable)	41			

Statistical analyses

No statistical analyses for this end point

Secondary: preliminary evaluation of anti-tumor activity

End point title	preliminary evaluation of anti-tumor activity

End point description:

End point type	Secondary

End point timeframe:

every 8 weeks until tumor progression

End point values	CetuGEX			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: millimeter(s)				
number (not applicable)	41			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events occurring after the patient entered the study until 28+2 days following the last infusion have been reported.us

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.1

Reporting groups

Reporting group title	Safety

Reporting group description:

The Intent-to-Treat (ITT) Population included any patient who was enrolled in a cohort and received any amount of study drug.

Serious adverse events	Safety		
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 41 (34.15%)		
number of deaths (all causes)	7		
number of deaths resulting from adverse events	4		
Vascular disorders			
Thrombosis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vena cava thrombosis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Death			

subjects affected / exposed	4 / 41 (9.76%)			
occurrences causally related to treatment / all	1 / 4			
deaths causally related to treatment / all	1 / 4			
General physical health deterioration				
subjects affected / exposed	5 / 41 (12.20%)			
occurrences causally related to treatment / all	4 / 6			
deaths causally related to treatment / all	0 / 0			
Stent malfunction				
subjects affected / exposed	1 / 41 (2.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	1 / 41 (2.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	1 / 41 (2.44%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Dysphagia				
subjects affected / exposed	1 / 41 (2.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	1 / 41 (2.44%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

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

Non-serious adverse events	Safety		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	41 / 41 (100.00%)		
Investigations			
Blood magnesium decreased			
subjects affected / exposed	5 / 41 (12.20%)		
occurrences (all)	17		
C-reactive protein increased			
subjects affected / exposed	5 / 41 (12.20%)		
occurrences (all)	5		
Vascular disorders			
Oedema peripheral			
subjects affected / exposed	9 / 41 (21.95%)		
occurrences (all)	13		
Nervous system disorders			
Dizziness			
subjects affected / exposed	6 / 41 (14.63%)		
occurrences (all)	7		
General disorders and administration site conditions			
Nausea			
subjects affected / exposed	13 / 41 (31.71%)		
occurrences (all)	32		
Vomiting			
subjects affected / exposed	12 / 41 (29.27%)		
occurrences (all)	32		
ECOG status worsened			
subjects affected / exposed	12 / 41 (29.27%)		
occurrences (all)	22		
Fatigue			
subjects affected / exposed	11 / 41 (26.83%)		
occurrences (all)	20		
Asthenia			
subjects affected / exposed	9 / 41 (21.95%)		
occurrences (all)	19		
Pyrexia			
subjects affected / exposed	9 / 41 (21.95%)		
occurrences (all)	14		

General physical health deterioration subjects affected / exposed occurrences (all)	5 / 41 (12.20%) 6		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	7 / 41 (17.07%) 15		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all)	 10 / 41 (24.39%) 14 8 / 41 (19.51%) 10 7 / 41 (17.07%) 8		
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all)	 10 / 41 (24.39%) 16 10 / 41 (24.39%) 15		
Skin and subcutaneous tissue disorders Acne subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all) Dermatitis acneiform subjects affected / exposed occurrences (all) dry skin	 10 / 41 (24.39%) 23 12 / 41 (29.27%) 30 10 / 41 (24.39%) 33		

subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all)	6 / 41 (14.63%) 7 5 / 41 (12.20%) 9		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all)	 9 / 41 (21.95%) 13 7 / 41 (17.07%) 14		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	 6 / 41 (14.63%) 10 6 / 41 (14.63%) 8		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) Hypokalaemia subjects affected / exposed occurrences (all)	 8 / 41 (19.51%) 10 6 / 41 (14.63%) 20		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported