Clinical trial results:
Randomized, controlled, open label, multicenter, phase II study to evaluate the efficacy and safety of CetuGEX plus chemotherapy in comparison to cetuximab plus chemotherapy for the treatment of patients with stage III/IV recurrent and/or metastatic squamous cell carcinoma of the head and neck

Summary

EudraCT number	2013-003695-13
Trial protocol	DE ES IT BE PL
Global end of trial date	04 October 2017

Results information

Result version number	v1 (current)
This version publication date	16 December 2020
First version publication date	16 December 2020

Trial information

Trial identification

Sponsor protocol code	GEXMab52201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02052960
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. Isabelle Ahrens-Fath, Glycotope GmbH, +49 30 94892610, Isabelle.Ahrens-Fath@glycotope.com
Scientific contact	Dr. Isabelle Ahrens-Fath, Glycotope GmbH, +49 30 94892610, Isabelle.Ahrens-Fath@glycotope.com
Sponsor organisation name	Glycotope GmbH
Sponsor organisation address	Robert Roessle St 10, Berlin, Germany, 13125
Public contact	Reception desk, Glycotope GmbH, +49 3094892600, Trials@glycotope.com
Scientific contact	Reception desk, Glycotope GmbH, +49 3094892600, Trials@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	No

1901/2006 apply to this trial?	

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	16 May 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 August 2017
Global end of trial reached?	Yes
Global end of trial date	04 October 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate the efficacy of CetuGEX™ for the treatment of patients with stage III/IV recurrent and/or metastatic squamous cell carcinoma of the head and neck (SCCHN) as compared to cetuximab (both in combination with platinum-based chemotherapy) in terms of progression-free survival (PFS).

Protection of trial subjects:

An independent DSMB was established, whose task was to review periodically the relevant safety data and provide advice on the continuation, modification or termination of the study. The DSMB comprised 3 members, 2 of them being oncologists and 1 of them a statistician. A study-specific charter defined in detail the composition, responsibilities, and procedures of the DSMB (Appendix 16.1.1). As soon as at least 10 patients per treatment arm had completed the second cycle of first line treatment, a first meeting of DSMB was scheduled to review the patient safety data. After this, regular 6-monthly meetings were scheduled until all ongoing patients had been treated for at least 6 months. Starting at the second DSMB meeting, in addition to review of patient safety data a descriptive analysis on progression and survival was included to monitor a potential detrimental effect of the IMP. For important reasons, additional meetings could be scheduled by the coordinating investigator, sponsor, medical monitor, or DSMB members for as long as patients were at risk.

Background therapy:

Eligible patients were randomized to receive as first line treatment either CetuGEX™ or cetuximab in combination with chemotherapy (5-FU and cisplatin) for the maximum duration of 6 cycles of combined treatment. In case of toxicity, chemotherapy could be dose reduced, discontinued or, if later than the first cycle, switched to carboplatin.
Single-agent maintenance therapy was continued with an unchanged dosing schedule until progression of disease or limiting toxicity

Evidence for comparator:

Cetuximab (Erbitux®) is a chimeric immunoglobulin G (IgG) 1 mouse-human antibody targeted against the extracellular domain of the epidermal growth factor receptor (EGFR) with high specificity and affinity and is produced in the murine myeloma cell line SP2/0.
Cetuximab is approved for use in combination with radiation therapy for treating squamous cell carcinoma of the head and neck (SCCHN) or in combination with platinum-based chemotherapy and 5-fluorouracil (5-FU) for the treatment of recurrent and/or metastatic SCCHN.

Actual start date of recruitment	27 February 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	24 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 58
Country: Number of subjects enrolled	Spain: 12
Country: Number of subjects enrolled	Belgium: 13
Country: Number of subjects enrolled	France: 44
Country: Number of subjects enrolled	Germany: 62
Country: Number of subjects enrolled	Italy: 8
Country: Number of subjects enrolled	Romania: 43
Worldwide total number of subjects	240
EEA total number of subjects	240

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)	177
From 65 to 84 years	63
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Between 27 Feb 2014 and 25 Jan 2016 a total of 321 patients (100.0%) were screened.
Date of first enrollment: 27 Feb 2014

Pre-assignment

Screening details:

Patients aged at least 18 years, with histologically confirmed recurrent and/or metastatic SCCHN not eligible for local treatment were enrolled in this study.

Period 1

Period 1 title	Treatment period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

No blinding

Arms

Are arms mutually exclusive?	Yes
Arm title	CetuGEX

Arm description:

CetuGEX™, chimeric monoclonal immunoglobulin G (IgG) antibody with fully human glycosylation; solution for intravenous infusion, provided in single-use vials.

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

Dosage and administration details:

The IMP CetuGEX™ was administered as infusion to all patients randomized to the CetuGEX™ arm, once weekly, starting with Day 0. Starting with the second infusion (Day 8 of Cycle 1), a time window of ± 1 day was allowed for the weekly infusions (calculated from the previous infusion).
The initial dose was 990 mg and subsequent doses were 720 mg once weekly. The initial loading dose was given as split-dose over 2 days with a priming dose of 60 mg on Day 0 diluted to a total volume of 100 mL (administered over 2 hours with a 30-minute break) and the remaining dose of 930 mg on Day 1 diluted to a total volume 500 mL (the intravenous infusion lasted for approximately 4 hours).

Arm title	Cetuximab

Arm description:

Cetuximab, chimeric monoclonal IgG antibody; solution for intravenous infusion, provided in single-use vials.

Arm type	Active comparator
Investigational medicinal product name	Cetuximab
Investigational medicinal product code	SUB31982
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cetuximab was administered once weekly as infusion to all patients randomized to the cetuximab arm.

Starting with the second infusion (Day 8 of Cycle 1), a time window of ± 1 day was allowed for the weekly infusions (calculated from the previous infusion). The initial dose was 400 mg/m2 body surface area (BSA) and each subsequent dose was 250 mg/m2 BSA. The maximum Infusion rate for the initial dose could not exceed 5 mg/min. The maximum infusion rate for subsequent doses could not exceed 10 mg/min. The BSA was calculated using the Mosteller formula:
BSA [m2] = (Weight [kg] × Height [cm]/3600)½

Number of subjects in period 1	CetuGEX	Cetuximab
Started	117	123
Completed	59	74
Not completed	58	49
Consent withdrawn by subject	6	11
Adverse event, non-fatal	19	17
still on treatment	4	3
unspecified	25	15
Protocol deviation	4	3

Baseline characteristics

Reporting groups	
Reporting group title	CetuGEX
Reporting group description:	
CetuGEX™, chimeric monoclonal immunoglobulin G (IgG) antibody with fully human glycosylation; solution for intravenous infusion, provided in single-use vials.	
Reporting group title	Cetuximab
Reporting group description:	
Cetuximab, chimeric monoclonal IgG antibody; solution for intravenous infusion, provided in single-use vials.	

Reporting group values	CetuGEX	Cetuximab	Total
Number of subjects	117	123	240
Age categorical			
Units: Subjects			
Adults (18-64 years)	88	89	177
From 65-84 years	29	34	63
Age continuous			
Units: years			
arithmetic mean	59.8	59.8	
standard deviation	± 7.54	± 7.91	-
Gender categorical			
Units: Subjects			
Female	18	17	35
Male	99	106	205

Subject analysis sets	
Subject analysis set title	Safety population
Subject analysis set type	Safety analysis
Subject analysis set description:	
The safety population (SAF) included all patients who received at least one dose of trial medication. This population was used for safety analyses.	
Subject analysis set title	Intent to treat population
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The ITT population consisted of all randomized patients. The ITT population was the primary population for the efficacy analysis.	

Reporting group values	Safety population	Intent to treat population	
Number of subjects	237	240	
Age categorical			
Units: Subjects			
Adults (18-64 years)		177	
From 65-84 years		63	
Age continuous			
Units: years			
arithmetic mean		59.8	

standard deviation	±	± 7.72	

Gender categorical Units: Subjects			
Female		35	
Male		205	

End points

End points reporting groups

Reporting group title	CetuGEX

Reporting group description:

CetuGEX™, chimeric monoclonal immunoglobulin G (IgG) antibody with fully human glycosylation; solution for intravenous infusion, provided in single-use vials.

Reporting group title	Cetuximab

Reporting group description:

Cetuximab, chimeric monoclonal IgG antibody; solution for intravenous infusion, provided in single-use vials.

Subject analysis set title	Safety population
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety population (SAF) included all patients who received at least one dose of trial medication. This population was used for safety analyses.

Subject analysis set title	Intent to treat population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The ITT population consisted of all randomized patients. The ITT population was the primary population for the efficacy analysis.

Primary: Progression free survival

End point title	Progression free survival

End point description:

The primary objective of the study was to evaluate the efficacy of CetuGEX™ for the treatment of patients with stage III/IV recurrent and/or metastatic squamous cell carcinoma of the head and neck (SCCHN) as compared to cetuximab (both in combination with platinum-based chemotherapy) in terms of progression-free survival (PFS).

End point type	Primary

End point timeframe:

The PFS was defined as time from randomization until disease progression or death of any cause.

End point values	CetuGEX	Cetuximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	117	123		
Units: weeks				
median (confidence interval 95%)	27.571 (23.429 to 33.571)	26.429 (24.714 to 31.286)		

Statistical analyses

Statistical analysis title	Log-Rank Test and Kaplan-Meier Analysis
Comparison groups	CetuGEX v Cetuximab

Number of subjects included in analysis	240
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8167
Method	Logrank
Confidence interval	
sides	2-sided

Secondary: Objective response rate

End point title	Objective response rate

End point description:

Objective response rate is the portion of patients with a tumor size reduction of a predefined amount for a minimum time period and it is defined as the sum of partial responses and complete responses.

End point type	Secondary

End point timeframe:

Time from randomization until disease progression or death, whichever occurs first

End point values	CetuGEX	Cetuximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	117	123		
Units: patients	52	57		

Statistical analyses

Statistical analysis title	Chi-square test
Comparison groups	CetuGEX v Cetuximab
Number of subjects included in analysis	240
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.768
Method	Chi-squared
Parameter estimate	rate difference
Point estimate	-1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.5
upper limit	10.7

Secondary: Clinical Benefit Rate

End point title	Clinical Benefit Rate

End point description:

The clinical benefit rate is the portion of patients with an objective response or stable disease.

End point type	Secondary

End point timeframe:

Time from randomization until disease progression or death, whichever occurs first.
SD: follow-up measurements must have met the SD criteria at least once after randomization at a minimum interval of 8 weeks

End point values	CetuGEX	Cetuximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	117	123		
Units: Subjects	88	94		

Statistical analyses

Statistical analysis title	Chi-square test
Comparison groups	Cetuximab v CetuGEX
Number of subjects included in analysis	240
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8269
Method	Chi-squared
Parameter estimate	rate difference
Point estimate	-1.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.05
upper limit	9.63

Secondary: Response duration

End point title	Response duration

End point description:

Duration of response, defined as the interval between the date of first response and the date of first progression (modified irRC) or death

End point type	Secondary

End point timeframe:

Response duration is measured from the time of initial response until documented tumor progression.

End point values	CetuGEX	Cetuximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	57		
Units: weeks				
median (confidence interval 95%)	26.143 (21.571 to 34.857)	30.143 (24.286 to 37.000)		

Statistical analyses

Statistical analysis title	Log-Rank Test and Kaplan-Meier Analysis
Comparison groups	CetuGEX v Cetuximab
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8663
Method	Logrank

Secondary: Overall survival

End point title	Overall survival

End point description:

The overall survival is defined as the duration of time from randomization to the time of death.

End point type	Secondary

End point timeframe:

Duration of time from randomization to the time of death.

End point values	CetuGEX	Cetuximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	117	123		
Units: weeks				
median (confidence interval 95%)	49.714 (40.714 to 73.857)	59.000 (52.857 to 70.286)		

Statistical analyses

Statistical analysis title	Log-Rank Test and Kaplan-Meier Analysis
Comparison groups	CetuGEX v Cetuximab

Number of subjects included in analysis	240
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9616
Method	Logrank

Secondary: Time to treatment failure

End point title	Time to treatment failure

End point description:

Time to treatment failure is defined as the time from randomization to treatment discontinuation for any reason, including disease progression, treatment toxicity, patient preference, or death

End point type	Secondary

End point timeframe:

Time to treatment failure, defined as the interval between the date of randomization and the date of treatment discontinuation for any reason

End point values	CetuGEX	Cetuximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	116	123		
Units: weeks				
median (confidence interval 95%)	22.143 (17.000 to 25.714)	23.286 (16.143 to 25.571)		

Statistical analyses

Statistical analysis title	Log-Rank Test and Kaplan-Meier Analysis
Comparison groups	CetuGEX v Cetuximab
Number of subjects included in analysis	239
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7038
Method	Logrank

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from the time of signing the ICF through the Safety Follow-Up Visit performed for all patients at 28 days (+ 2 days) after the last dose administered.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16

Reporting groups

Reporting group title	Safety population

Reporting group description:

The safety population included all patients who received at least 1 dose of trial medication. This population was used for safety analyses.

Reporting group title	CetuGEX Safety population

Reporting group description: -

Reporting group title	Cetuximab Safety population

Reporting group description: -

Serious adverse events	Safety population	CetuGEX Safety population	Cetuximab Safety population
Total subjects affected by serious adverse events			
subjects affected / exposed	148 / 237 (62.45%)	70 / 115 (60.87%)	78 / 122 (63.93%)
number of deaths (all causes)	34	20	14
number of deaths resulting from adverse events	34	20	14
Investigations			
Blood creatinine increased			
subjects affected / exposed	5 / 237 (2.11%)	2 / 115 (1.74%)	3 / 122 (2.46%)
occurrences causally related to treatment / all	0 / 5	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	5 / 237 (2.11%)	3 / 115 (2.61%)	2 / 122 (1.64%)
occurrences causally related to treatment / all	3 / 5	3 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	3 / 237 (1.27%)	2 / 115 (1.74%)	1 / 122 (0.82%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 2	0 / 2	0 / 0

Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	3 / 237 (1.27%)	2 / 115 (1.74%)	1 / 122 (0.82%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 2	0 / 1	0 / 1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	18 / 237 (7.59%)	9 / 115 (7.83%)	9 / 122 (7.38%)
occurrences causally related to treatment / all	0 / 22	0 / 10	0 / 12
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Neutropenia			
subjects affected / exposed	15 / 237 (6.33%)	8 / 115 (6.96%)	7 / 122 (5.74%)
occurrences causally related to treatment / all	0 / 17	0 / 8	0 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	6 / 237 (2.53%)	2 / 115 (1.74%)	4 / 122 (3.28%)
occurrences causally related to treatment / all	5 / 9	2 / 2	3 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	5 / 237 (2.11%)	3 / 115 (2.61%)	2 / 122 (1.64%)
occurrences causally related to treatment / all	0 / 7	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	5 / 237 (2.11%)	1 / 115 (0.87%)	4 / 122 (3.28%)
occurrences causally related to treatment / all	0 / 6	0 / 1	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	4 / 237 (1.69%)	2 / 115 (1.74%)	2 / 122 (1.64%)
occurrences causally related to treatment / all	1 / 4	1 / 2	0 / 2
deaths causally related to treatment / all	1 / 4	1 / 2	0 / 2
General physical health deterioration			

subjects affected / exposed	4 / 237 (1.69%)	2 / 115 (1.74%)	2 / 122 (1.64%)
occurrences causally related to treatment / all	0 / 6	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Device dislocation			
subjects affected / exposed	3 / 237 (1.27%)	1 / 115 (0.87%)	2 / 122 (1.64%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	3 / 237 (1.27%)	2 / 115 (1.74%)	1 / 122 (0.82%)
occurrences causally related to treatment / all	1 / 3	0 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucosal inflammation			
subjects affected / exposed	3 / 237 (1.27%)	3 / 115 (2.61%)	0 / 122 (0.00%)
occurrences causally related to treatment / all	2 / 3	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	5 / 237 (2.11%)	3 / 115 (2.61%)	2 / 122 (1.64%)
occurrences causally related to treatment / all	2 / 5	1 / 3	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	5 / 237 (2.11%)	3 / 115 (2.61%)	2 / 122 (1.64%)
occurrences causally related to treatment / all	0 / 7	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	4 / 237 (1.69%)	2 / 115 (1.74%)	2 / 122 (1.64%)
occurrences causally related to treatment / all	0 / 5	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	5 / 237 (2.11%)	2 / 115 (1.74%)	3 / 122 (2.46%)
occurrences causally related to treatment / all	4 / 5	2 / 2	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Renal and urinary disorders			
Renal failure			
subjects affected / exposed	3 / 237 (1.27%)	2 / 115 (1.74%)	1 / 122 (0.82%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Renal failure acute			
subjects affected / exposed	3 / 237 (1.27%)	1 / 115 (0.87%)	2 / 122 (1.64%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	21 / 237 (8.86%)	12 / 115 (10.43%)	9 / 122 (7.38%)
occurrences causally related to treatment / all	10 / 25	6 / 15	4 / 10
deaths causally related to treatment / all	0 / 8	0 / 6	0 / 2
Sepsis			
subjects affected / exposed	10 / 237 (4.22%)	3 / 115 (2.61%)	7 / 122 (5.74%)
occurrences causally related to treatment / all	1 / 10	0 / 3	1 / 7
deaths causally related to treatment / all	1 / 2	0 / 0	1 / 2
Device related infection			
subjects affected / exposed	9 / 237 (3.80%)	5 / 115 (4.35%)	4 / 122 (3.28%)
occurrences causally related to treatment / all	0 / 10	0 / 5	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung abscess			
subjects affected / exposed	3 / 237 (1.27%)	0 / 115 (0.00%)	3 / 122 (2.46%)
occurrences causally related to treatment / all	0 / 3	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	9 / 237 (3.80%)	4 / 115 (3.48%)	5 / 122 (4.10%)
occurrences causally related to treatment / all	0 / 9	0 / 4	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypomagnesaemia			

subjects affected / exposed	9 / 237 (3.80%)	4 / 115 (3.48%)	5 / 122 (4.10%)
occurrences causally related to treatment / all	8 / 9	0 / 4	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	7 / 237 (2.95%)	3 / 115 (2.61%)	4 / 122 (3.28%)
occurrences causally related to treatment / all	4 / 10	1 / 5	3 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Decreased appetite			
subjects affected / exposed	5 / 237 (2.11%)	2 / 115 (1.74%)	3 / 122 (2.46%)
occurrences causally related to treatment / all	1 / 5	0 / 2	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Safety population	CetuGEX Safety population	Cetuximab Safety population
Total subjects affected by non-serious adverse events			
subjects affected / exposed	235 / 237 (99.16%)	114 / 115 (99.13%)	121 / 122 (99.18%)
Vascular disorders			
Hypotension			
subjects affected / exposed	32 / 237 (13.50%)	16 / 115 (13.91%)	16 / 122 (13.11%)
occurrences (all)	44	20	24
Hypertension			
subjects affected / exposed	19 / 237 (8.02%)	11 / 115 (9.57%)	8 / 122 (6.56%)
occurrences (all)	43	30	13
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	79 / 237 (33.33%)	41 / 115 (35.65%)	38 / 122 (31.15%)
occurrences (all)	163	82	81
Asthenia			
subjects affected / exposed	71 / 237 (29.96%)	34 / 115 (29.57%)	37 / 122 (30.33%)
occurrences (all)	135	60	75
Mucosal inflammation			
subjects affected / exposed	60 / 237 (25.32%)	24 / 115 (20.87%)	36 / 122 (29.51%)
occurrences (all)	108	45	63
Pyrexia			

subjects affected / exposed	40 / 237 (16.88%)	16 / 115 (13.91%)	24 / 122 (19.67%)
occurrences (all)	47	17	30
Chills			
subjects affected / exposed	32 / 237 (13.50%)	26 / 115 (22.61%)	6 / 122 (4.92%)
occurrences (all)	34	28	6
General physical health deterioration			
subjects affected / exposed	13 / 237 (5.49%)	7 / 115 (6.09%)	6 / 122 (4.92%)
occurrences (all)	16	10	6
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	25 / 237 (10.55%)	10 / 115 (8.70%)	15 / 122 (12.30%)
occurrences (all)	31	10	21
Dyspnoea			
subjects affected / exposed	25 / 237 (10.55%)	11 / 115 (9.57%)	14 / 122 (11.48%)
occurrences (all)	33	17	16
Epistaxis			
subjects affected / exposed	16 / 237 (6.75%)	6 / 115 (5.22%)	10 / 122 (8.20%)
occurrences (all)	20	7	13
Psychiatric disorders			
Insomnia			
subjects affected / exposed	12 / 237 (5.06%)	8 / 115 (6.96%)	4 / 122 (3.28%)
occurrences (all)	18	13	5
Investigations			
Weight decreased			
subjects affected / exposed	81 / 237 (34.18%)	42 / 115 (36.52%)	39 / 122 (31.97%)
occurrences (all)	155	83	72
Blood creatinine increased			
subjects affected / exposed	19 / 237 (8.02%)	11 / 115 (9.57%)	8 / 122 (6.56%)
occurrences (all)	34	19	15
Platelet count decreased			
subjects affected / exposed	13 / 237 (5.49%)	7 / 115 (6.09%)	6 / 122 (4.92%)
occurrences (all)	19	13	6
Cardiac disorders			
Tachycardia			
subjects affected / exposed	13 / 237 (5.49%)	10 / 115 (8.70%)	3 / 122 (2.46%)
occurrences (all)	14	11	3

Nervous system disorders			
Dizziness			
subjects affected / exposed	29 / 237 (12.24%)	14 / 115 (12.17%)	15 / 122 (12.30%)
occurrences (all)	36	16	20
Headache			
subjects affected / exposed	26 / 237 (10.97%)	13 / 115 (11.30%)	13 / 122 (10.66%)
occurrences (all)	35	16	19
Neuropathy peripheral			
subjects affected / exposed	12 / 237 (5.06%)	3 / 115 (2.61%)	9 / 122 (7.38%)
occurrences (all)	23	4	19
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	100 / 237 (42.19%)	44 / 115 (38.26%)	56 / 122 (45.90%)
occurrences (all)	256	104	152
Neutropenia			
subjects affected / exposed	98 / 237 (41.35%)	47 / 115 (40.87%)	51 / 122 (41.80%)
occurrences (all)	229	105	124
Leukopenia			
subjects affected / exposed	70 / 237 (29.54%)	33 / 115 (28.70%)	37 / 122 (30.33%)
occurrences (all)	188	98	90
Thrombocytopenia			
subjects affected / exposed	47 / 237 (19.83%)	21 / 115 (18.26%)	26 / 122 (21.31%)
occurrences (all)	117	48	69
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	23 / 237 (9.70%)	11 / 115 (9.57%)	12 / 122 (9.84%)
occurrences (all)	25	13	12
Tinnitus			
subjects affected / exposed	14 / 237 (5.91%)	8 / 115 (6.96%)	6 / 122 (4.92%)
occurrences (all)	17	10	7
Hearing impaired			
subjects affected / exposed	13 / 237 (5.49%)	6 / 115 (5.22%)	7 / 122 (5.74%)
occurrences (all)	14	6	8
Eye disorders			
Conjunctivitis			
subjects affected / exposed	19 / 237 (8.02%)	10 / 115 (8.70%)	9 / 122 (7.38%)
occurrences (all)	28	16	12

Gastrointestinal disorders			
Nausea			
subjects affected / exposed	121 / 237 (51.05%)	58 / 115 (50.43%)	63 / 122 (51.64%)
occurrences (all)	284	122	162
Diarrhoea			
subjects affected / exposed	79 / 237 (33.33%)	38 / 115 (33.04%)	41 / 122 (33.61%)
occurrences (all)	157	73	84
Vomiting			
subjects affected / exposed	76 / 237 (32.07%)	35 / 115 (30.43%)	41 / 122 (33.61%)
occurrences (all)	150	67	83
Constipation			
subjects affected / exposed	57 / 237 (24.05%)	34 / 115 (29.57%)	23 / 122 (18.85%)
occurrences (all)	87	47	40
Stomatitis			
subjects affected / exposed	38 / 237 (16.03%)	26 / 115 (22.61%)	12 / 122 (9.84%)
occurrences (all)	87	66	21
Dysphagia			
subjects affected / exposed	31 / 237 (13.08%)	15 / 115 (13.04%)	16 / 122 (13.11%)
occurrences (all)	42	20	22
Dyspepsia			
subjects affected / exposed	28 / 237 (11.81%)	15 / 115 (13.04%)	13 / 122 (10.66%)
occurrences (all)	42	23	19
Abdominal pain			
subjects affected / exposed	19 / 237 (8.02%)	7 / 115 (6.09%)	12 / 122 (9.84%)
occurrences (all)	30	17	13
Abdominal pain upper			
subjects affected / exposed	15 / 237 (6.33%)	9 / 115 (7.83%)	6 / 122 (4.92%)
occurrences (all)	17	11	6
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	91 / 237 (38.40%)	44 / 115 (38.26%)	47 / 122 (38.52%)
occurrences (all)	243	116	127
Dermatitis acneiform			
subjects affected / exposed	51 / 237 (21.52%)	30 / 115 (26.09%)	21 / 122 (17.21%)
occurrences (all)	170	106	64
Dry skin			

subjects affected / exposed	43 / 237 (18.14%)	20 / 115 (17.39%)	23 / 122 (18.85%)
occurrences (all)	49	23	26
Skin fissures			
subjects affected / exposed	36 / 237 (15.19%)	19 / 115 (16.52%)	17 / 122 (13.93%)
occurrences (all)	74	38	36
Acne			
subjects affected / exposed	21 / 237 (8.86%)	10 / 115 (8.70%)	11 / 122 (9.02%)
occurrences (all)	63	23	40
Alopecia			
subjects affected / exposed	20 / 237 (8.44%)	9 / 115 (7.83%)	11 / 122 (9.02%)
occurrences (all)	23	10	13
Erythema			
subjects affected / exposed	16 / 237 (6.75%)	8 / 115 (6.96%)	8 / 122 (6.56%)
occurrences (all)	18	8	10
Pruritus			
subjects affected / exposed	14 / 237 (5.91%)	10 / 115 (8.70%)	4 / 122 (3.28%)
occurrences (all)	22	16	6
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	16 / 237 (6.75%)	5 / 115 (4.35%)	11 / 122 (9.02%)
occurrences (all)	23	7	16
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	13 / 237 (5.49%)	6 / 115 (5.22%)	7 / 122 (5.74%)
occurrences (all)	17	9	8
Infections and infestations			
Paronychia			
subjects affected / exposed	28 / 237 (11.81%)	16 / 115 (13.91%)	12 / 122 (9.84%)
occurrences (all)	55	36	19
Pneumonia			
subjects affected / exposed	25 / 237 (10.55%)	13 / 115 (11.30%)	12 / 122 (9.84%)
occurrences (all)	31	17	14
Urinary tract infection			
subjects affected / exposed	13 / 237 (5.49%)	7 / 115 (6.09%)	6 / 122 (4.92%)
occurrences (all)	19	12	7
Bronchitis			

subjects affected / exposed	12 / 237 (5.06%)	3 / 115 (2.61%)	9 / 122 (7.38%)
occurrences (all)	17	3	14
Device related infection			
subjects affected / exposed	12 / 237 (5.06%)	8 / 115 (6.96%)	4 / 122 (3.28%)
occurrences (all)	13	8	5
Sepsis			
subjects affected / exposed	12 / 237 (5.06%)	4 / 115 (3.48%)	8 / 122 (6.56%)
occurrences (all)	12	4	8
Metabolism and nutrition disorders			
Hypomagnesaemia			
subjects affected / exposed	104 / 237 (43.88%)	53 / 115 (46.09%)	51 / 122 (41.80%)
occurrences (all)	327	146	181
Decreased appetite			
subjects affected / exposed	66 / 237 (27.85%)	36 / 115 (31.30%)	30 / 122 (24.59%)
occurrences (all)	95	47	48
Hypokalaemia			
subjects affected / exposed	42 / 237 (17.72%)	20 / 115 (17.39%)	22 / 122 (18.03%)
occurrences (all)	88	35	53
Dehydration			
subjects affected / exposed	23 / 237 (9.70%)	10 / 115 (8.70%)	13 / 122 (10.66%)
occurrences (all)	25	11	14
Hypocalcaemia			
subjects affected / exposed	23 / 237 (9.70%)	10 / 115 (8.70%)	13 / 122 (10.66%)
occurrences (all)	39	19	20
Hyponatraemia			
subjects affected / exposed	20 / 237 (8.44%)	11 / 115 (9.57%)	9 / 122 (7.38%)
occurrences (all)	23	14	9

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 February 2015	Modification to the inclusion criteria such that patients with squamous cell carcinoma of the head and neck could be included irrespective of their EGFR status, rather than restricting inclusion to EGFR-positive patients. In addition, patients' p16 status was removed from the stratification criteria. The EGFR status was added as a subgroup for analysis of secondary endpoints, and an exploration of the effects of both EGFR status and p16 status was added to the sensitivity analyses.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported