Clinical trial results:
Randomized, Placebo-Controlled, Double Blind Phase 2 Study of Patritumab (U3-1287) in Combination with Cetuximab plus Platinum Based Therapy in First Line Setting in Subjects with Recurrent or Metastatic Squamous Cell Carcinoma of the Head and Neck

Summary

EudraCT number	2015-002222-40
Trial protocol	GB DE HU BE
Global end of trial date	21 February 2018

Results information

Result version number	v1 (current)
This version publication date	21 September 2018
First version publication date	21 September 2018

Trial information

Trial identification

Sponsor protocol code	U31287-A-U203

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02633800
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Daiichi Sankyo, Inc.
Sponsor organisation address	211 Mt. Airy Road, Basking Ridge, New Jersey, United States, 07920
Public contact	Clinical Study Director, Daiichi Sankyo , Inc., 1 9089926400,
Scientific contact	Clinical Study Director, Daiichi Sankyo , Inc., 1 9089926400,

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	05 April 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 February 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial is to evaluate progression-free survival (PFS) in the heregulin (HRG) high expression population from subjects treated with patritumab + cetuximab + platinum-based therapy compared to placebo + cetuximab + platinum-based therapy.

Protection of trial subjects:

This trial was conducted in accordance with the ethical principles of Good Clinical Practice, according to the ICH Harmonised Tripartite Guideline.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 December 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	Poland: 5
Country: Number of subjects enrolled	Romania: 4
Country: Number of subjects enrolled	United Kingdom: 14
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	France: 21
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Hungary: 39
Worldwide total number of subjects	87
EEA total number of subjects	87

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	59
From 65 to 84 years	28
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Of 125 screened, 87 patients from 8 countries were randomized into treatment groups

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Patritumab

Arm description:

Patritumab + cetuximab + cisplatin or carboplatin

Arm type	Experimental
Investigational medicinal product name	Patritumab
Investigational medicinal product code	
Other name	U3-1287, Monoclonal antibody
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patritumab + cetuximab + cisplatin or carboplatin

Arm title	Placebo

Arm description:

Placebo + cetuximab + cisplatin or carboplatin

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Placebo comparator
Pharmaceutical forms	Solution for infusion in administration system
Routes of administration	Intravenous use

Dosage and administration details:

Placebo + cetuximab + cisplatin or carboplatin

Number of subjects in period 1	Patritumab	Placebo
Started	44	43
Completed	0	0
Not completed	44	43
Clinical progression	3	6
Consent withdrawn by subject	-	3
Radiological progression	-	23
Adverse event, non-fatal	7	2
Death	3	3
Patient request	1	1
Study terminated by sponsor	6	5
Radiologic progression	23	-
Reason not provided	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Patritumab
Reporting group description: Patritumab + cetuximab + cisplatin or carboplatin	

Reporting group title	Placebo
Reporting group description: Placebo + cetuximab + cisplatin or carboplatin	

Reporting group values	Patritumab	Placebo	Total
Number of subjects	44	43	87
Age categorical Units: Subjects			
Adults (18-64 years)	32	27	59
From 65-84 years	12	16	28
Age continuous Units: years			
arithmetic mean	57.3	61.0	
standard deviation	± 9.18	± 9.19	-
Gender categorical Units: Subjects			
Female	8	7	15
Male	36	36	72
Baseline Eastern Cooperative Oncology Group (ECOG) Performance Status			
The baseline value is defined as the last non-missing value before initial administration of study treatment.			
Units: Subjects			
0=Fully active	19	22	41
1=Restricted in Physically Strenuous Activity	25	20	45
2=Ambulatory and Capable of All Self-Care	0	1	1
3=Capable of Only Limited Self Care	0	0	0
4=Completely Disabled	0	0	0

End points

End points reporting groups

Reporting group title	Patritumab

Reporting group description:

Patritumab + cetuximab + cisplatin or carboplatin

Reporting group title	Placebo

Reporting group description:

Placebo + cetuximab + cisplatin or carboplatin

Primary: Progression free survival (PFS) in the heregulin (HRG)-high expression population

End point title	Progression free survival (PFS) in the heregulin (HRG)-high expression population

End point description:

PFS is defined as the time from the date of randomization to the date of the first radiographic disease progression or death
due to any cause, whichever comes first.

Median PFS is from Kaplan-Meier analysis. CI for median was computed using Brookmeyer-Crowley method.

End point type	Primary

End point timeframe:

until radiological progression or death (or at study termination)

End point values	Patritumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	25		
Units: months				
median (confidence interval 95%)	5.56 (4.08 to 11.18)	5.56 (3.06 to 8.29)		

Statistical analyses

Statistical analysis title	Heregulin-high population - Patritumab vs Placebo

Statistical analysis description:

Both Log-rank test and Cox regression analysis did not adjust stratification factors.

Comparison groups	Patritumab v Placebo

Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8342 [1]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.9291
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4856
upper limit	1.7778

Notes:

[1] - Unstratified Log-rank p-value

Secondary: Overall survival (OS)

End point title	Overall survival (OS)

End point description:

Overall survival could not be analyzed with the data available at trial termination.

End point type	Secondary

End point timeframe:

Date of randomization to death due to any cause

End point values	Patritumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: months				
median (confidence interval 95%)	(to)	(to)		

Notes:

[2] - The trial terminated before sufficient data were collected for this analysis.

[3] - The trial terminated before sufficient data were collected for this analysis.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse events were collected until trial termination at 12 months.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups	
Reporting group title	Patritumab + Cetuximab + Platinum Based Therapy
Reporting group description: -	
Reporting group title	Placebo + Cetuximab + Platinum Based Therapy
Reporting group description: -	

Serious adverse events	Patritumab + Cetuximab + Platinum Based Therapy	Placebo + Cetuximab + Platinum Based Therapy	
Total subjects affected by serious adverse events			
subjects affected / exposed	19 / 44 (43.18%)	16 / 43 (37.21%)	
number of deaths (all causes)	24	20	
number of deaths resulting from adverse events	5	7	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant pleural effusion			
subjects affected / exposed	1 / 44 (2.27%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour haemorrhage			
subjects affected / exposed	0 / 44 (0.00%)	4 / 43 (9.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Tumour pain			
subjects affected / exposed	2 / 44 (4.55%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	0 / 44 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	0 / 44 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Localised oedema			
subjects affected / exposed	1 / 44 (2.27%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 44 (2.27%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	0 / 44 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic shock			
subjects affected / exposed	0 / 44 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	1 / 44 (2.27%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acquired tracheo-oesophageal fistula			
subjects affected / exposed	1 / 44 (2.27%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Dyspnoea			
subjects affected / exposed	1 / 44 (2.27%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 44 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Lower respiratory tract congestion			
subjects affected / exposed	0 / 44 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia aspiration			
subjects affected / exposed	1 / 44 (2.27%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 44 (2.27%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary Embolism			
subjects affected / exposed	0 / 44 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	1 / 44 (2.27%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Investigations			
Ejection Fraction Decreased			
subjects affected / exposed	1 / 44 (2.27%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutrophil count decreased			

subjects affected / exposed	0 / 44 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	1 / 44 (2.27%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 44 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head Injury			
subjects affected / exposed	0 / 44 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute Coronary Syndrome			
subjects affected / exposed	0 / 44 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac Disorder			
subjects affected / exposed	0 / 44 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	0 / 44 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

Cardiovascular insufficiency			
subjects affected / exposed	1 / 44 (2.27%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Myocardial ischaemia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus tachycardia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 44 (2.27%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			
subjects affected / exposed	0 / 44 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 44 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 44 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 44 (2.27%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 44 (2.27%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 44 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	1 / 44 (2.27%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 44 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral pain			
subjects affected / exposed	1 / 44 (2.27%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	0 / 44 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 44 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal Impairment			
subjects affected / exposed	1 / 44 (2.27%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Osteonecrosis			
subjects affected / exposed	1 / 44 (2.27%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Arthritis bacterial			
subjects affected / exposed	1 / 44 (2.27%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter site infection			
subjects affected / exposed	1 / 44 (2.27%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	2 / 44 (4.55%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Empyema			
subjects affected / exposed	1 / 44 (2.27%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			

subjects affected / exposed	0 / 44 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphangitis			
subjects affected / exposed	1 / 44 (2.27%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	4 / 44 (9.09%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 7	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Sepsis			
subjects affected / exposed	0 / 44 (0.00%)	2 / 43 (4.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	0 / 44 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Decreased Appetite			
subjects affected / exposed	0 / 44 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	3 / 44 (6.82%)	2 / 43 (4.65%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	0 / 44 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			

subjects affected / exposed	1 / 44 (2.27%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	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	Patritumab + Cetuximab + Platinum Based Therapy	Placebo + Cetuximab + Platinum Based Therapy	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	44 / 44 (100.00%)	42 / 43 (97.67%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 44 (4.55%)	3 / 43 (6.98%)	
occurrences (all)	2	4	
Hypotension			
subjects affected / exposed	3 / 44 (6.82%)	4 / 43 (9.30%)	
occurrences (all)	3	5	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	10 / 44 (22.73%)	11 / 43 (25.58%)	
occurrences (all)	14	17	
Chills			
subjects affected / exposed	4 / 44 (9.09%)	2 / 43 (4.65%)	
occurrences (all)	5	2	
Fatigue			
subjects affected / exposed	11 / 44 (25.00%)	7 / 43 (16.28%)	
occurrences (all)	14	9	
Mucosal inflammation			
subjects affected / exposed	8 / 44 (18.18%)	2 / 43 (4.65%)	
occurrences (all)	13	2	
Oedema peripheral			

subjects affected / exposed	1 / 44 (2.27%)	3 / 43 (6.98%)	
occurrences (all)	1	3	
Pyrexia			
subjects affected / exposed	4 / 44 (9.09%)	1 / 43 (2.33%)	
occurrences (all)	7	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 44 (11.36%)	5 / 43 (11.63%)	
occurrences (all)	7	5	
Dyspnoea			
subjects affected / exposed	7 / 44 (15.91%)	5 / 43 (11.63%)	
occurrences (all)	12	8	
Haemoptysis			
subjects affected / exposed	4 / 44 (9.09%)	3 / 43 (6.98%)	
occurrences (all)	5	3	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 44 (4.55%)	3 / 43 (6.98%)	
occurrences (all)	2	3	
Depression			
subjects affected / exposed	2 / 44 (4.55%)	3 / 43 (6.98%)	
occurrences (all)	2	3	
Insomnia			
subjects affected / exposed	4 / 44 (9.09%)	4 / 43 (9.30%)	
occurrences (all)	4	6	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 44 (6.82%)	2 / 43 (4.65%)	
occurrences (all)	6	2	
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 44 (6.82%)	1 / 43 (2.33%)	
occurrences (all)	5	1	
Blood alkaline phosphatase increased			
subjects affected / exposed	3 / 44 (6.82%)	0 / 43 (0.00%)	
occurrences (all)	6	0	
Neutrophil count decreased			

subjects affected / exposed	0 / 44 (0.00%)	3 / 43 (6.98%)	
occurrences (all)	0	4	
Weight Decreased			
subjects affected / exposed	11 / 44 (25.00%)	10 / 43 (23.26%)	
occurrences (all)	16	12	
Weight increased			
subjects affected / exposed	1 / 44 (2.27%)	3 / 43 (6.98%)	
occurrences (all)	1	5	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	3 / 44 (6.82%)	0 / 43 (0.00%)	
occurrences (all)	5	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 44 (9.09%)	2 / 43 (4.65%)	
occurrences (all)	4	2	
Dysgeusia			
subjects affected / exposed	4 / 44 (9.09%)	0 / 43 (0.00%)	
occurrences (all)	4	0	
Headache			
subjects affected / exposed	3 / 44 (6.82%)	5 / 43 (11.63%)	
occurrences (all)	4	6	
Paraesthesia			
subjects affected / exposed	3 / 44 (6.82%)	0 / 43 (0.00%)	
occurrences (all)	3	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	18 / 44 (40.91%)	13 / 43 (30.23%)	
occurrences (all)	34	22	
Leukocytosis			
subjects affected / exposed	5 / 44 (11.36%)	0 / 43 (0.00%)	
occurrences (all)	5	0	
Neutropenia			
subjects affected / exposed	13 / 44 (29.55%)	11 / 43 (25.58%)	
occurrences (all)	23	22	
Thrombocytopenia			

subjects affected / exposed	10 / 44 (22.73%)	14 / 43 (32.56%)	
occurrences (all)	20	39	
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	4 / 44 (9.09%)	2 / 43 (4.65%)	
occurrences (all)	4	2	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	7 / 44 (15.91%)	5 / 43 (11.63%)	
occurrences (all)	7	7	
Diarrhoea			
subjects affected / exposed	12 / 44 (27.27%)	5 / 43 (11.63%)	
occurrences (all)	18	6	
Dysphagia			
subjects affected / exposed	8 / 44 (18.18%)	4 / 43 (9.30%)	
occurrences (all)	10	4	
Gastrooesophageal Reflux Disease			
subjects affected / exposed	4 / 44 (9.09%)	2 / 43 (4.65%)	
occurrences (all)	4	2	
Nausea			
subjects affected / exposed	16 / 44 (36.36%)	14 / 43 (32.56%)	
occurrences (all)	23	22	
Oral Pain			
subjects affected / exposed	3 / 44 (6.82%)	1 / 43 (2.33%)	
occurrences (all)	3	1	
Stomatitis			
subjects affected / exposed	5 / 44 (11.36%)	3 / 43 (6.98%)	
occurrences (all)	9	3	
Vomiting			
subjects affected / exposed	9 / 44 (20.45%)	7 / 43 (16.28%)	
occurrences (all)	11	14	
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	15 / 44 (34.09%)	8 / 43 (18.60%)	
occurrences (all)	20	17	
Dry skin			

subjects affected / exposed	6 / 44 (13.64%)	7 / 43 (16.28%)	
occurrences (all)	7	8	
Pruritus			
subjects affected / exposed	3 / 44 (6.82%)	3 / 43 (6.98%)	
occurrences (all)	3	3	
Rash			
subjects affected / exposed	20 / 44 (45.45%)	21 / 43 (48.84%)	
occurrences (all)	42	28	
Rash Maculo-Papular			
subjects affected / exposed	3 / 44 (6.82%)	2 / 43 (4.65%)	
occurrences (all)	5	2	
Skin fissures			
subjects affected / exposed	7 / 44 (15.91%)	6 / 43 (13.95%)	
occurrences (all)	8	13	
Skin toxicity			
subjects affected / exposed	0 / 44 (0.00%)	3 / 43 (6.98%)	
occurrences (all)	0	3	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	4 / 44 (9.09%)	1 / 43 (2.33%)	
occurrences (all)	4	1	
Neck pain			
subjects affected / exposed	3 / 44 (6.82%)	4 / 43 (9.30%)	
occurrences (all)	6	10	
Pain in extremity			
subjects affected / exposed	0 / 44 (0.00%)	3 / 43 (6.98%)	
occurrences (all)	0	3	
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	6 / 44 (13.64%)	4 / 43 (9.30%)	
occurrences (all)	6	5	
Folliculitis			
subjects affected / exposed	2 / 44 (4.55%)	5 / 43 (11.63%)	
occurrences (all)	3	6	
Paronychia			

subjects affected / exposed	15 / 44 (34.09%)	4 / 43 (9.30%)	
occurrences (all)	25	4	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	11 / 44 (25.00%)	11 / 43 (25.58%)	
occurrences (all)	14	17	
Hypercalcaemia			
subjects affected / exposed	3 / 44 (6.82%)	3 / 43 (6.98%)	
occurrences (all)	3	3	
Hypokalaemia			
subjects affected / exposed	11 / 44 (25.00%)	2 / 43 (4.65%)	
occurrences (all)	15	5	
Hypomagnesaemia			
subjects affected / exposed	16 / 44 (36.36%)	15 / 43 (34.88%)	
occurrences (all)	29	35	
Hyponatraemia			
subjects affected / exposed	3 / 44 (6.82%)	1 / 43 (2.33%)	
occurrences (all)	4	1	
Hypophosphataemia			
subjects affected / exposed	2 / 44 (4.55%)	5 / 43 (11.63%)	
occurrences (all)	6	12	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 August 2015	- Added sample collections for additional biomarkers - Revised text on contraception based on Medicines and Healthcare products Regulatory Agency (MHRA) feedback
29 January 2016	- Added assessments, exclusions and clarified procedural details to enhance patient safety and welfare - Adjusted text as needed to ensure using local standard of care for the chemotherapy is acceptable per protocol.
14 June 2016	- Changes made to reflect the recommendation by European Regulatory Authorities for new guidance regarding maintenance dose modification or suspension of patritumab treatment for possible effects on cardiac function, and the addition of three new exclusion criteria - Removed sentence that does not include full details for patritimab infusion bag instructions. Full/revised instructions are provided in a separate updated Pharmacy Manual: "The selected dose of patritumab/placebo regimen will be diluted in 5% dextrose in a final volume of 100 mL." - Added paragraph noting that left ventricular ejection fraction (LVEF) will be monitored throughout the study and that dose modifications in patritumab will be according to guidance in Table 5.1, and ejection fraction Withhold Criteria and Discontinuation Criteria for patritumab are more precisely defined Administrative change of sponsoring entity to a different Daiichi Sankyo company.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
21 February 2018	Trial was terminated by sponsor due to lack of efficacy.	-

Notes:

Limitations and caveats

None reported