Clinical trial results:
A Single-Arm, Multicenter, Phase 1b Study with an Expansion Cohort to Evaluate Safety and Efficacy of Necitumumab in Combination with Abemaciclib in Treatment of Patients with Stage IV Non-Small Cell Lung Cancer (NSCLC)

Summary

EudraCT number	2014-005042-21
Trial protocol	BE ES
Global end of trial date	28 May 2019

Results information

Result version number	v2 (current)
This version publication date	24 February 2021
First version publication date	07 June 2020
Version creation reason	• Correction of full data set Copy Correction to full data set

Trial information

Trial identification

Sponsor protocol code	I4X-MC-JFCU

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02411591
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 15573

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 877CTLilly,
Scientific contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 8772854559,

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	28 May 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 May 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This is medical research evaluating the safety and efficacy of two new medicines (necitumumab and abemaciclib), administered in combination in participants affected by a defined type of advanced lung cancer (stage IV non-small-cell lung cancer).

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 June 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	24 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 11
Country: Number of subjects enrolled	France: 52
Country: Number of subjects enrolled	Spain: 3
Worldwide total number of subjects	66
EEA total number of subjects	66

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)	40
From 65 to 84 years	25
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

No Text Available

Pre-assignment

Screening details:

The study has 2 parts (Part A and Part B). Part A is a dose-escalation study to determine the recommended dose of abemaciclib in combination with necitumumab Part B (expansion cohort). Completers completed the 2 cycles, with required assessment, had progressive disease or died due to any cause, alive and on study at conclusion but off treatment.

Period 1

Period 1 title	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	Cohort 1 (Necitumumab 800 mg + Abemaciclib 100 mg)

Arm description:

Part A: Necitumumab 800 milligram (mg) was administered IV on Days 1 and 8, followed by abemaciclib 100 mg given orally every 12 hours on Days 1 to 21. (21 day cycles.) Treatment may continue until discontinuation criterion is met.

Arm type	Experimental
Investigational medicinal product name	Necitumumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Necitumumab 800 milligram (mg) was administered intravenously (IV) on Days 1 and 8.

Investigational medicinal product name	Abemaciclib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

abemaciclib 100 mg given orally every 12 hours on Days 1 to 21.

Arm title	Cohort 2 (Necitumumab 800 mg + Abemaciclib 150 mg)

Arm description:

Part A: Necitumumab 800 mg administered intravenously (IV) on Days 1 and 8, followed by abemaciclib 150 mg given orally every 12 hours on Days 1 to 21. (21 day cycles.) Treatment may continue until discontinuation criterion is met.

Part B: (expansion cohort): Necitumumab 800 mg administered IV on Days 1 and 8, followed by abemaciclib 150 mg given orally every 12 hours on Days 1 to 21. (21 day cycles.) Treatment may continue until discontinuation criterion is met.

Arm type	Experimental

Investigational medicinal product name	Necitumumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Necitumumab administered intravenously (IV) on Days 1 and 8, followed by abemaciclib given orally every 12 hours on Days 1 to 21. (21 day cycles.)

Investigational medicinal product name	Abemaciclib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

abemaciclib 150 mg given orally every 12 hours on Days 1 to 21.

Arm title	Cohort 3 (Necitumumab 800 mg + Abemaciclib 200 mg)

Arm description:

Part A: Necitumumab 800 mg was administered IV on Days 1 and 8, followed by abemaciclib 200 mg given orally every 12 hours on Days 1 to 21. (21 day cycles.) Treatment may continue until discontinuation criterion is met.

Arm type	Experimental
Investigational medicinal product name	Necitumumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Necitumumab 800 mg was administered IV on Days 1 and 8.

Investigational medicinal product name	Abemaciclib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

abemaciclib 200 mg given orally every 12 hours on Days 1 to 21.

Number of subjects in period 1	Cohort 1 (Necitumumab 800 mg + Abemaciclib 100 mg)	Cohort 2 (Necitumumab 800 mg + Abemaciclib 150 mg)	Cohort 3 (Necitumumab 800 mg + Abemaciclib 200 mg)
Started	3	57	6
Part A	3	6 [1]	6
Expansion Cohort Part B	0 [2]	51	0 [3]
Progressive Disease	3	42 [4]	3
Death	0 [5]	2 [6]	0 [7]
Completed	3	47	3
Not completed	0	10	3
Consent withdrawn by subject	-	3	-

Physician decision	-	3	1
Adverse event, non-fatal	-	4	2

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The number of participants at each milestone is a subset analysis population to the overall number of participants in the arm.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The number of participants at each milestone is a subset analysis population to the overall number of participants in the arm.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The number of participants at each milestone is a subset analysis population to the overall number of participants in the arm.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The number of participants at each milestone is a subset analysis population to the overall number of participants in the arm.

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The number of participants at each milestone is a subset analysis population to the overall number of participants in the arm.

[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The number of participants at each milestone is a subset analysis population to the overall number of participants in the arm.

[7] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The number of participants at each milestone is a subset analysis population to the overall number of participants in the arm.

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1 (Necitumumab 800 mg + Abemaciclib 100 mg)
Reporting group description:	
Part A: Necitumumab 800 milligram (mg) was administered IV on Days 1 and 8, followed by abemaciclib 100 mg given orally every 12 hours on Days 1 to 21. (21 day cycles.) Treatment may continue until discontinuation criterion is met.	
Reporting group title	Cohort 2 (Necitumumab 800 mg + Abemaciclib 150 mg)
Reporting group description:	
Part A: Necitumumab 800 mg administered intravenously (IV) on Days 1 and 8, followed by abemaciclib 150 mg given orally every 12 hours on Days 1 to 21. (21 day cycles.) Treatment may continue until discontinuation criterion is met. Part B: (expansion cohort): Necitumumab 800 mg administered IV on Days 1 and 8, followed by abemaciclib 150 mg given orally every 12 hours on Days 1 to 21. (21 day cycles.) Treatment may continue until discontinuation criterion is met.	
Reporting group title	Cohort 3 (Necitumumab 800 mg + Abemaciclib 200 mg)
Reporting group description:	
Part A: Necitumumab 800 mg was administered IV on Days 1 and 8, followed by abemaciclib 200 mg given orally every 12 hours on Days 1 to 21. (21 day cycles.) Treatment may continue until discontinuation criterion is met.	

Reporting group values	Cohort 1 (Necitumumab 800 mg + Abemaciclib 100 mg)	Cohort 2 (Necitumumab 800 mg + Abemaciclib 150 mg)	Cohort 3 (Necitumumab 800 mg + Abemaciclib 200 mg)
Number of subjects	3	57	6
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	62.33	61.42	49.00
standard deviation	± 2.31	± 10.58	± 7.59
Gender categorical Units: Subjects			
Female	1	17	1
Male	2	40	5
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	2	0
Not Hispanic or Latino	1	13	1
Unknown or Not Reported	2	42	5
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	1	16	1
More than one race	0	0	0

Unknown or Not Reported	2	41	5
Region of Enrollment Units: Subjects			
Belgium	1	9	1
France	2	45	5
Spain	0	3	0

Reporting group values	Total		
Number of subjects	66		
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	- -		
Gender categorical Units: Subjects			
Female	19		
Male	47		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2		
Not Hispanic or Latino	15		
Unknown or Not Reported	49		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	0		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	0		
White	18		
More than one race	0		
Unknown or Not Reported	48		
Region of Enrollment Units: Subjects			
Belgium	11		
France	52		
Spain	3		

End points

End points reporting groups

Reporting group title	Cohort 1 (Necitumumab 800 mg + Abemaciclib 100 mg)

Reporting group description:

Part A: Necitumumab 800 milligram (mg) was administered IV on Days 1 and 8, followed by abemaciclib 100 mg given orally every 12 hours on Days 1 to 21. (21 day cycles.) Treatment may continue until discontinuation criterion is met.

Reporting group title	Cohort 2 (Necitumumab 800 mg + Abemaciclib 150 mg)

Reporting group description:

Part A: Necitumumab 800 mg administered intravenously (IV) on Days 1 and 8, followed by abemaciclib 150 mg given orally every 12 hours on Days 1 to 21. (21 day cycles.) Treatment may continue until discontinuation criterion is met.

Part B: (expansion cohort): Necitumumab 800 mg administered IV on Days 1 and 8, followed by abemaciclib 150 mg given orally every 12 hours on Days 1 to 21. (21 day cycles.) Treatment may continue until discontinuation criterion is met.

Reporting group title	Cohort 3 (Necitumumab 800 mg + Abemaciclib 200 mg)

Reporting group description:

Part A: Necitumumab 800 mg was administered IV on Days 1 and 8, followed by abemaciclib 200 mg given orally every 12 hours on Days 1 to 21. (21 day cycles.) Treatment may continue until discontinuation criterion is met.

Subject analysis set title	Cohort 3 (Necitumamab 800 mg + Abemaciclib 200 mg)
Subject analysis set type	Per protocol

Subject analysis set description:

Part A: Necitumumab 800 mg was administered IV on Days 1 and 8, followed by abemaciclib 200 mg given orally every 12 hours on Days 1 to 21. (21 day cycles.) Treatment may continue until discontinuation criterion is met.

Subject analysis set title	Total Enrolled Participants (Necitumumab + Abemaciclib)
Subject analysis set type	Per protocol

Subject analysis set description:

Cohorts 1, 2 and 3 combined. Necitumumab 800 mg was administered IV on Days 1 and 8, followed by abemaciclib 100 mg, 150 mg or 200 mg given orally every 12 hours on Days 1 to 21. (21 day cycles.) Treatment may continue until discontinuation criterion is met.

Subject analysis set title	Necitumumab
Subject analysis set type	Per protocol

Subject analysis set description:

Necitumumab 800 mg was administered IV on Days 1 and 8, of a 3-week cycle.

Subject analysis set title	Abemaciclib 100 mg
Subject analysis set type	Per protocol

Subject analysis set description:

Necitumumab 800 mg administered IV on Days 1 and 8 followed by abemaciclib 100 mg given orally every 12 hours on Days 1 to 21. (21 day cycles.) Treatment may continue until discontinuation criterion is met.

Subject analysis set title	Abemaciclib 150 mg
Subject analysis set type	Per protocol

Subject analysis set description:

Necitumumab 800 mg administered IV on Days 1 and 8 followed by abemaciclib 150 mg given orally every 12 hours on Days 1 to 21. (21 day cycles.) Treatment may continue until discontinuation criterion is met.

Subject analysis set title	Abemaciclib 200 mg
Subject analysis set type	Per protocol

Subject analysis set description:

Necitumumab 800 mg administered IV on Days 1 and 8 followed by abemaciclib 200 mg given orally every 12 hours on Days 1 to 21. (21 day cycles.) Treatment may continue until discontinuation criterion is met.

Subject analysis set title	Cohort 1 (Necitumumab 800 mg + Abemaciclib 100 mg)
Subject analysis set type	Per protocol

Subject analysis set description:

Part A: Necitumumab 800 mg was administered IV on Days 1 and 8, followed by abemaciclib 100 mg given orally every 12 hours on Days 1 to 21. (21 day cycles.) Treatment may continue until discontinuation criterion is met.

Subject analysis set title	Cohort 2 (Necitumumab 800 mg + Abemaciclib 150 mg)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Part A: Necitumumab 800 mg was administered IV on Days 1 and 8, followed by abemaciclib 150 mg given orally every 12 hours on Days 1 to 21. (21 day cycles.)

Primary: Part A: Number of Participants with Abemaciclib Dose Limiting Toxicities (DLTs)

End point title	Part A: Number of Participants with Abemaciclib Dose Limiting Toxicities (DLTs)[1]

End point description:

A DLT was defined as one of the following adverse events (AEs), occurring in Cycle 1 if considered to be definitely, probably, or possibly related to necitumumab and abemaciclib: Grade 3 or 4 nonhematologic toxicity according to the National Cancer Institute Common Terminology Criteria for Adverse Events Version 4.0 (NCI-CTCAE v4.0), except for nausea, vomiting, diarrhea, or electrolyte disturbance. Grade 3 or 4 nausea, vomiting, or diarrhea that persists more than 2 days despite maximal supportive intervention. Grade 3 thrombocytopenia with bleeding requiring transfusion. Grade 4 thrombocytopenia with or without bleeding. Grade 4 neutropenia that persists more than 5 days.

End point type	Primary

End point timeframe:

Baseline through Cycle 1 (Up to 21 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: DLT endpoint was summarized using descriptive statistics.

End point values	Cohort 3 (Necitumamab 800 mg + Abemaciclib 200 mg)	Cohort 1 (Necitumumab 800 mg + Abemaciclib 100 mg)	Cohort 2 (Necitumumab 800 mg + Abemaciclib 150 mg)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	3[2]	6[3]	6[4]	
Units: participants	0	1	3	

Notes:

[2] - All participants who received at least one dose of study drug and had evaluable DLTs.

[3] - All participants who received at least one dose of study drug and had evaluable DLTs.

[4] - All participants who received at least one dose of study drug and had evaluable DLTs.

Statistical analyses

No statistical analyses for this end point

Primary: Progression Free Survival (PFS) Rate at 3 Months (Percentage of Participants with PFS at 3 Months)

End point title	Progression Free Survival (PFS) Rate at 3 Months (Percentage of Participants with PFS at 3 Months)[5]

End point description:

PFS defined as time from baseline until first radiographic documentation of measured progressive disease(PD) defined by response evaluation criteria in solid tumors (RECIST) v1.1 or death from any cause.PD was at least 20% increase in sum of diameters of target lesions with reference being smallest sum on study and an absolute increase of at least 5 millimeter (mm) or unequivocal progression of non-

target lesions,or 1 or more new lesions.If participant does not have complete baseline disease assessment,PFS time censored at date of randomization,regardless of whether or not objectively determined disease progression or death observed for participant.If participant was not known to have died or have objective progression as of data inclusion cutoff date for analysis, the PFS time censored at last adequate tumor assessment date. The use of new anticancer therapy prior to occurrence of PD resulted in censoring at the date of last radiographic assessment prior to initiation of new therapy.

End point type	Primary

End point timeframe:

Baseline to measured progressive disease or death due to any cause (3 Months)

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: PFS endpoint was summarized using descriptive statistics.

End point values	Cohort 1 (Necitumumab 800 mg + Abemaciclib 100 mg)	Cohort 2 (Necitumumab 800 mg + Abemaciclib 150 mg)	Cohort 3 (Necitumumab 800 mg + Abemaciclib 200 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3[6]	57[7]	6[8]	
Units: Percentage of Participants				
number (confidence interval 95%)	66.7 (5.4 to 94.5)	32.3 (20.4 to 44.8)	50.0 (11.1 to 80.4)	

Notes:

[6] - All enrolled participants who received at least one dose of study drug and had evaluable PFS data.

[7] - All enrolled participants who received at least one dose of study drug and had evaluable PFS data.

[8] - All enrolled participants who received at least one dose of study drug and had evaluable PFS data.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Achieve Best Overall Tumor Response of Complete or Partial Response (Objective Response Rate [ORR])

End point title	Percentage of Participants Who Achieve Best Overall Tumor Response of Complete or Partial Response (Objective Response Rate [ORR])

End point description:

ORR was the percentage of participants achieving a best overall response of complete response (CR) or partial response (PR) as per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1. CR defined as the disappearance of all target and non-target lesions and no appearance of new lesions. PR defined as at least a 30% decrease in the sum of the longest diameters (LD) of target lesions (taking as reference the baseline sum LD), no progression of nontarget lesions, and no appearance of new lesions. PD was at least a 20% increase in the sum of the diameters of target lesions, with reference being the smallest sum on study and an absolute increase of at least 5 mm, or unequivocal progression of non-target lesions, or 1 or more new lesions. Confidence intervals are based on Clopper-Pearson method.

End point type	Secondary

End point timeframe:

Baseline to measured progressive disease or start of new anti-cancer therapy (up to 21 months)

End point values	Cohort 1 (Necitumumab 800 mg + Abemaciclib 100 mg)	Cohort 2 (Necitumumab 800 mg + Abemaciclib 150 mg)	Cohort 3 (Necitumumab 800 mg + Abemaciclib 200 mg)	Total Enrolled Participants (Necitumumab + Abemaciclib)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	3[9]	57[10]	6[11]	66[12]
Units: percentage of participants				
number (confidence interval 95%)				
Overall Response Rate	66.7 (9.4 to 99.2)	5.3 (1.1 to 14.6)	0.0 (0.0 to 45.9)	7.6 (2.5 to 16.8)
PR	66.7 (9.4 to 99.2)	5.3 (1.1 to 14.6)	0.0 (0.0 to 45.9)	7.6 (2.5 to 16.8)
SD	33.3 (0.8 to 90.6)	42.1 (29.1 to 55.9)	66.7 (22.3 to 95.7)	43.9 (31.7 to 56.7)
PD	0.0 (0.0 to 70.8)	47.4 (34.0 to 61.0)	16.7 (0.4 to 64.1)	42.4 (30.3 to 55.2)

Notes:

[9] - All enrolled participants who received at least one dose of study drug and had evaluable ORR data.

[10] - All enrolled participants who received at least one dose of study drug and had evaluable ORR data.

[11] - All enrolled participants who received at least one dose of study drug and had evaluable ORR data.

[12] - All enrolled participants who received at least one dose of study drug and had evaluable ORR data.

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK): Predose Concentration (Cmin) of Necitumumab

End point title	Pharmacokinetics (PK): Predose Concentration (Cmin) of Necitumumab

End point description:

Predose necitumumab concentration data following doses of 800 mg administered Day 1 and 8 of a 3-week cycle as an intravenous (IV) infusion over 60 minutes.

End point type	Secondary

End point timeframe:

Cycle 1, Day 8 (C1D8) and C2,3,5,7 D1: Predose

End point values	Necitumumab			
Subject group type	Subject analysis set			
Number of subjects analysed	61[13]			
Units: microgram/milliliter (µg/mL)				
geometric mean (standard deviation)				
Cycle 1, Day 8	64.1 (± 43.1)			
Cycle 2, Day 1	49.6 (± 63.8)			
Cycle 3, Day 1	93.8 (± 44.1)			
Cycle 5, Day 1	160 (± 50.3)			
Cycle 7, Day 1	165 (± 42.1)			

Notes:

[13] - All participants who received at least one dose of necitumumab and had evaluable PK data.

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK): Maximum Concentration (Cmax) of Necitumumab

End point title	Pharmacokinetics (PK): Maximum Concentration (Cmax) of Necitumumab

End point description:

Maximum necitumumab concentration data following doses of 800 mg administered Day 1 and 8 of a 3-week cycle as an intravenous (IV) infusion over 60 minutes.

End point type	Secondary

End point timeframe:

Cycle 1, Day 1 (C1D1): 0.25, 2,4,10 hours(h) post dose, C1D8: 0.25h post dose, Cycle 2, Day 1 (C2D1): 0.25, 2,4,10h post dose; C3,5,7 D1: 0.25h post dose

End point values	Necitumumab			
Subject group type	Subject analysis set			
Number of subjects analysed	61[14]			
Units: µg/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1, Day 1	228 (± 45.6)			
Cycle 1, Day 8 (D8)	304 (± 21.9)			
Cycle 2, Day 1	270 (± 25.6)			
Cycle 3, Day 1	318 (± 43.7)			
Cycle 5, Day 1	356 (± 42.7)			
Cycle 7, Day 1	350 (± 24.7)			

Notes:

[14] - Geometric coefficient of variation is presented as a percent.

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK): Maximum Concentration (Cmax) of Abemaciclib

End point title	Pharmacokinetics (PK): Maximum Concentration (Cmax) of Abemaciclib

End point description:

Pharmacokinetics (PK): Maximum Concentration (Cmax) of Abemaciclib summary of LSN3106729 noncompartmental PK parameters after twice daily oral dose of Abemaciclib.

End point type	Secondary

End point timeframe:

Cycle 1, Day 1 (C1D1): 0.25, 2,4,6,8,10 hours(h) post dose, C1D8: 0.25h post dose, C2D1: 0.25, 2,4,6,8,10h post dose; C3,5,7 D1: 0.25h post dose

End point values	Abemaciclib 100 mg	Abemaciclib 150 mg	Abemaciclib 200 mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	3[15]	5[16]	5[17]	
Units: nanogram/milliliter (ng/mL)				
geometric mean (geometric coefficient of variation)	15.6 (± 146)	26 (± 148)	38.2 (± 80)	

Notes:

[15] - Geometric coefficient of variation is presented as a percent.

[16] - Geometric coefficient of variation is presented as a percent.

[17] - Geometric coefficient of variation is presented as a percent.

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK): Area Under the Concentration Time Curve (AUC) From Zero to the Last Time Point (AUC[0-tlast]) Abemaciclib

End point title	Pharmacokinetics (PK): Area Under the Concentration Time Curve (AUC) From Zero to the Last Time Point (AUC[0-tlast]) Abemaciclib

End point description:

Pharmacokinetics (PK): Area Under the Concentration Time Curve (AUC) From Zero to the Last Time Point (AUC[0-tlast]) summary of LSN3106729 noncompartmental PK parameters after twice daily oral dose of Abemaciclib. (tlast = 10 hours)

End point type	Secondary

End point timeframe:

Cycle 1, Day 1 (C1D1): 0.25, 2,4,6,8,10 hours(h) post dose

End point values	Abemaciclib 100 mg	Abemaciclib 150 mg	Abemaciclib 200 mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	3[18]	5[19]	5[20]	
Units: hour*nanogram/milliliter (hr*ng/mL)				
geometric mean (geometric coefficient of variation)	118 (± 200)	209 (± 136)	336 (± 83)	

Notes:

[18] - Geometric coefficient of variation is presented as a percent.

[19] - Geometric coefficient of variation is presented as a percent.

[20] - Geometric coefficient of variation is presented as a percent.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With a Best Overall Response of Complete Response (CR), Partial Response (PR), and Stable Disease (SD) (Disease Control Rate [DCR])

End point title	Percentage of Participants With a Best Overall Response of Complete Response (CR), Partial Response (PR), and Stable Disease (SD) (Disease Control Rate [DCR])

End point description:

Disease Control Rate (DCR) is defined as the percentage of participants achieving a best overall response of stable disease (SD), PR, or CR. DCR used the same denominator as defined in ORR. Among participants counted in the denominator, the numerator counted those with a confirmed best tumor response of SD, PR, or CR per RECIST v1.1. Confidence intervals are based on Clopper-Pearson method.

End point type	Secondary

End point timeframe:

Baseline to measured progressive disease or start of new anti-cancer therapy (up to 21 months)

End point values	Cohort 1 (Necitumumab 800 mg + Abemaciclib 100 mg)	Cohort 2 (Necitumumab 800 mg + Abemaciclib 150 mg)	Cohort 3 (Necitumumab 800 mg + Abemaciclib 200 mg)	Total Enrolled Participants (Necitumumab + Abemaciclib)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	3[21]	57[22]	6[23]	66
Units: percentage of participants				
number (confidence interval 95%)	100 (29.2 to 100.0)	47.4 (34.0 to 61.0)	66.7 (22.3 to 95.7)	51.5 (38.9 to 64.0)

Notes:

[21] - All enrolled participants who received at least one dose of study drug and had evaluable ORR data.
[22] - All enrolled participants who received at least one dose of study drug and had evaluable ORR data.
[23] - All enrolled participants who received at least one dose of study drug and had evaluable ORR data.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Overall survival (OS) is defined as the time from the date of study enrollment to the date of death from any cause. For each participant who is not known to have died as of the data -inclusion cutoff date for a particular analysis, OS was censored for that analysis at the last known alive date.

End point type	Secondary

End point timeframe:

Baseline to date of death from any cause (24 Months)

End point values	Cohort 1 (Necitumumab 800 mg + Abemaciclib 100 mg)	Cohort 2 (Necitumumab 800 mg + Abemaciclib 150 mg)	Cohort 3 (Necitumumab 800 mg + Abemaciclib 200 mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3[24]	57[25]	6[26]	
Units: Months				
median (confidence interval 95%)	9999 (18.20 to 9999)	6.93 (4.96 to 12.85)	13.45 (1.31 to 18.53)	

Notes:

[24] - 9999 = NA due to 95% Confidence Interval (CI) had not matured yet and median was not calculable.

[25] - All enrolled participants who received at least one dose of study drug and had evaluable OS data.

[26] - All enrolled participants who received at least one dose of study drug and had evaluable OS data.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to 21 Months	
Adverse event reporting additional description: I4X-MC-JFCU	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups	
Reporting group title	Necitumumab-800mg Abemaciclib-150mg
Reporting group description: -	
Reporting group title	Necitumumab-800mg Abemaciclib-200mg
Reporting group description: -	
Reporting group title	Necitumumab-800mg Abemaciclib-100mg
Reporting group description: -	

Serious adverse events	Necitumumab-800mg Abemaciclib-150mg	Necitumumab-800mg Abemaciclib-200mg	Necitumumab-800mg Abemaciclib-100mg
Total subjects affected by serious adverse events			
subjects affected / exposed	25 / 57 (43.86%)	4 / 6 (66.67%)	2 / 3 (66.67%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	1	0	0
Vascular disorders			
phlebitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 57 (1.75%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
superior vena cava syndrome			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 57 (1.75%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
fatigue			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	2 / 57 (3.51%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
general physical health deterioration			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 57 (3.51%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pyrexia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 57 (3.51%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
vascular stent thrombosis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 57 (1.75%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
dyspnoea			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 57 (1.75%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumomediastinum			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 57 (1.75%)	0 / 6 (0.00%)	0 / 3 (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
pneumonitis			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	2 / 57 (3.51%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
pulmonary embolism			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 57 (1.75%)	0 / 6 (0.00%)	0 / 3 (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
Investigations			
blood creatinine increased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 57 (1.75%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
infusion related reaction			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
atrial flutter			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 57 (1.75%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
headache			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 57 (3.51%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
loss of consciousness			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	1 / 57 (1.75%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
somnolence			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 57 (1.75%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
thrombocytopenia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	1 / 6 (16.67%)	0 / 3 (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
Eye disorders			
blindness			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 57 (1.75%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
diarrhoea			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 57 (3.51%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
nausea			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 57 (1.75%)	0 / 6 (0.00%)	0 / 3 (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
vomiting			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	5 / 57 (8.77%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	5 / 6	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
cholecystitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
palmar-plantar erythrodysaesthesia syndrome			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 57 (1.75%)	0 / 6 (0.00%)	0 / 3 (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
Renal and urinary disorders			
acute kidney injury			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 57 (1.75%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hydronephrosis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	1 / 6 (16.67%)	0 / 3 (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
renal failure			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 57 (1.75%)	0 / 6 (0.00%)	0 / 3 (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
ureterolithiasis			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 57 (0.00%)	1 / 6 (16.67%)	0 / 3 (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			
anal abscess			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	1 / 6 (16.67%)	0 / 3 (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
device related infection			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 57 (1.75%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
erysipelas			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 57 (1.75%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
lung infection			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 57 (3.51%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumonia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 57 (1.75%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
respiratory tract infection			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 57 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
urinary tract infection			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 57 (1.75%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 57 (1.75%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypokalaemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 57 (1.75%)	0 / 6 (0.00%)	0 / 3 (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

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

Non-serious adverse events	Necitumumab-800mg Abemaciclib-150mg	Necitumumab-800mg Abemaciclib-200mg	Necitumumab-800mg Abemaciclib-100mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	57 / 57 (100.00%)	6 / 6 (100.00%)	3 / 3 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
pyogenic granuloma			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
tumour pain			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	5 / 57 (8.77%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	5	0	1
Vascular disorders			
hypotension			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 57 (1.75%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
intermittent claudication			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	8 / 57 (14.04%)	1 / 6 (16.67%)	1 / 3 (33.33%)
occurrences (all)	12	1	1
fatigue			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	29 / 57 (50.88%)	3 / 6 (50.00%)	2 / 3 (66.67%)
occurrences (all)	49	4	6
general physical health deterioration			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	4 / 57 (7.02%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
mucosal dryness			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
oedema peripheral			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 57 (5.26%)	1 / 6 (16.67%)	1 / 3 (33.33%)
occurrences (all)	3	1	1
pain			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	5 / 57 (8.77%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	5	0	0
pyrexia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	10 / 57 (17.54%)	2 / 6 (33.33%)	2 / 3 (66.67%)
occurrences (all)	10	2	3
xerosis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	4 / 57 (7.02%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	4	0	1
Reproductive system and breast disorders			
vaginal discharge			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed[1]	1 / 17 (5.88%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	10 / 57 (17.54%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	10	1	0
dysphonia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
dyspnoea			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	21 / 57 (36.84%)	1 / 6 (16.67%)	1 / 3 (33.33%)
occurrences (all)	21	3	1
epistaxis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	2 / 6 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	2	2
haemoptysis			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	3 / 57 (5.26%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
laryngeal inflammation			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
pleural effusion			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
anxiety			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	1 / 6 (16.67%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
depression			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
insomnia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	5 / 57 (8.77%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	5	0	0
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	5 / 57 (8.77%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	6	0	0
aspartate aminotransferase increased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 57 (5.26%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
blood creatinine increased			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	13 / 57 (22.81%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	23	1	0
neutrophil count decreased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	9 / 57 (15.79%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	18	0	0
platelet count decreased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	11 / 57 (19.30%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	28	1	0
weight decreased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	7 / 57 (12.28%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	9	2	0
Injury, poisoning and procedural complications			
contusion			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Cardiac disorders			
arrhythmia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
sinus tachycardia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 57 (3.51%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Nervous system disorders			
disturbance in attention			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
dysgeusia			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 57 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
headache			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	6 / 57 (10.53%)	3 / 6 (50.00%)	1 / 3 (33.33%)
occurrences (all)	6	3	1
paraesthesia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 57 (1.75%)	1 / 6 (16.67%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
peripheral sensory neuropathy			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 57 (1.75%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	21 / 57 (36.84%)	3 / 6 (50.00%)	1 / 3 (33.33%)
occurrences (all)	45	4	1
leukocytosis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
leukopenia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 57 (1.75%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
lymphopenia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 57 (5.26%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	3	1	0
thrombocytopenia			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	5 / 57 (8.77%)	2 / 6 (33.33%)	0 / 3 (0.00%)
occurrences (all)	9	2	0
Eye disorders			
cataract			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
dry eye			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
lacrimation increased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 57 (3.51%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	3	0	1
Gastrointestinal disorders			
abdominal pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	7 / 57 (12.28%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	7	0	0
abdominal pain upper			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 57 (5.26%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	3	1	0
ascites			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
constipation			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	8 / 57 (14.04%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	8	0	1
dental caries			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 57 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
diarrhoea			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	29 / 57 (50.88%)	3 / 6 (50.00%)	1 / 3 (33.33%)
occurrences (all)	49	6	1
dry mouth			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 57 (3.51%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
dysphagia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	4 / 57 (7.02%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
haemorrhoidal haemorrhage			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
nausea			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	24 / 57 (42.11%)	3 / 6 (50.00%)	0 / 3 (0.00%)
occurrences (all)	32	3	0
stomatitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	7 / 57 (12.28%)	3 / 6 (50.00%)	0 / 3 (0.00%)
occurrences (all)	8	5	0
tooth discolouration			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
vomiting			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	16 / 57 (28.07%)	3 / 6 (50.00%)	1 / 3 (33.33%)
occurrences (all)	24	4	1

Hepatobiliary disorders			
cholestasis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 57 (3.51%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Skin and subcutaneous tissue disorders			
dermatitis acneiform			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	26 / 57 (45.61%)	3 / 6 (50.00%)	2 / 3 (66.67%)
occurrences (all)	41	5	6
dry skin			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	15 / 57 (26.32%)	4 / 6 (66.67%)	2 / 3 (66.67%)
occurrences (all)	20	4	3
nail ridging			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 57 (1.75%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
palmar-plantar erythrodysaesthesia syndrome			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 57 (5.26%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	9	0	0
petechiae			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
pruritus			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	5 / 57 (8.77%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	7	0	1
rash			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	8 / 57 (14.04%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	23	1	0
rash maculo-papular			

alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	4 / 57 (7.02%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
skin fissures			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 57 (1.75%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	2
skin ulcer			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 57 (1.75%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Renal and urinary disorders			
dysuria			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
ureterolithiasis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
arthritis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 57 (1.75%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
back pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
bursitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
musculoskeletal pain			
alternative dictionary used:			

MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
neck pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
osteoporosis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
pain in extremity			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 57 (1.75%)	1 / 6 (16.67%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
Infections and infestations			
anal abscess			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
bronchitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	4 / 57 (7.02%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	5	0	0
conjunctivitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	5 / 57 (8.77%)	1 / 6 (16.67%)	1 / 3 (33.33%)
occurrences (all)	5	1	1
folliculitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	5 / 57 (8.77%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	8	1	0
fungal skin infection			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 57 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
nail infection			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	3
paronychia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	6 / 57 (10.53%)	3 / 6 (50.00%)	2 / 3 (66.67%)
occurrences (all)	9	3	3
pharyngitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
tinea pedis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
upper respiratory tract infection			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 57 (3.51%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
urinary tract infection			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 57 (5.26%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	21 / 57 (36.84%)	4 / 6 (66.67%)	2 / 3 (66.67%)
occurrences (all)	24	7	3
hyperglycaemia			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	1 / 57 (1.75%)	1 / 6 (16.67%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
hyperkalaemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 57 (5.26%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
hypoalbuminaemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	4 / 57 (7.02%)	2 / 6 (33.33%)	0 / 3 (0.00%)
occurrences (all)	4	2	0
hypocalcaemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 57 (1.75%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
hypochloraemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 57 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
hypokalaemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	12 / 57 (21.05%)	4 / 6 (66.67%)	1 / 3 (33.33%)
occurrences (all)	17	5	2
hypomagnesaemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	20 / 57 (35.09%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	29	3	0
hyponatraemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	4 / 57 (7.02%)	2 / 6 (33.33%)	0 / 3 (0.00%)
occurrences (all)	7	2	0
hypophosphataemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	8 / 57 (14.04%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	18	2	0

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 May 2016	Protocol amendment (b) overall changes are as follows: • Interim efficacy analyses (as needed) have been added to aid in the planning of future trials. • Specific adverse events of necitumumab have been amended. • The infusion time for necitumumab has been updated to 60 minutes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported