Clinical trial results:
SHERBOC: A Double-blind, Placebo-controlled, Phase 2 trial of Seribantumab Plus Fulvestrant in Postmenopausal Women with Hormone Receptor-positive, Heregulin Positive (HRG+), HER2 Negative Metastatic Breast Cancer Whose Disease Progressed After Prior Systemic Therapy

Summary

EudraCT number	2017-000565-76
Trial protocol	DE ES AT BE IT
Global end of trial date	30 November 2018

Results information

Result version number	v1 (current)
This version publication date	01 September 2021
First version publication date	01 September 2021

Trial information

Trial identification

Sponsor protocol code	MM-121-02-02-10

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03241810
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merrimack Pharmaceuticals Inc.
Sponsor organisation address	One Kendall Square, Cambridge, United States, MA 02139
Public contact	Regulatory Affairs, Merrimack Pharmaceuticals Inc., 001 6174417624, GenClin-Alert@merrimack.com
Scientific contact	Regulatory Affairs, Merrimack Pharmaceuticals Inc., 001 6174417624, GenClin-Alert@merrimack.com
Sponsor organisation name	Elevation Oncology
Sponsor organisation address	888 7th Ave., 12th Floor, New York, United States, 10106
Public contact	Valerie M. Jansen, MD, PhD, Elevation Oncology, 001 716 371 1125,
Scientific contact	Valerie M. Jansen, MD, PhD, Elevation Oncology, 001 716 371 1125,

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	30 November 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 November 2018
Global end of trial reached?	Yes
Global end of trial date	30 November 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to determine whether the combination of seribantumab + fulvestrant is more effective than placebo + fulvestrant based on investigator assessed Progression Free Survival (PFS) in HRG positive patients (defined as HRG ISH score of > or = to 1+)

Protection of trial subjects:

N/A

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 August 2017
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	Spain: 7
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	United States: 11
Country: Number of subjects enrolled	Canada: 1
Worldwide total number of subjects	22
EEA total number of subjects	10

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)	15
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

At the time of the study termination by the prior Sponsor (Merrimack Pharmaceuticals), 62 sites participated in the study (27 in North America and 36 in Europe).

Pre-assignment

Screening details:

Patients that have signed informed consent, identified as HRG positive based on centralized tissue analysis & have successfully completed study entry criteria (safety population-patients receiving at least one dose of study medication).

Pre-assignment period milestones

Number of subjects started	22
Number of subjects completed	22

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, Carer, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A (Experimental): Seribantumab and Fulvestrant

Arm description:

Seribantumab (a human monoclonal antibody that targets ErbB3, a cell surface receptor that is activated by the ligand heregulin. Heregulin-driven ErbB3 signaling has been implicated as a mechanism of tumor growth and resistance to targeted, cytotoxic and anti-endocrine therapies. When used in the combination setting, seribantumab is designed to block ErbB3 signaling in order to enhance the anti-tumor effect of a combination therapy partner): fixed dose of 3000 mg intravenously (IV) on day 1 and 15 of each 28-day cycle
Fulvestrant (a drug treatment of hormone receptor-positive metastatic breast cancer in post-menopausal women with disease progression following anti-estrogen therapy. It is an estrogen receptor antagonist with no agonist effects, which works both by down-regulating and by degrading the estrogen receptor): 500 mg intramuscularly (IM) on Days 1 and 15 of Cycle 1, and then on Day 1 of each subsequent 28 day cycle

Arm type	Experimental
Investigational medicinal product name	Seribantumab
Investigational medicinal product code	
Other name	MM-121
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Fixed dose of 3000 mg intravenously (IV) on day 1 and 15 of each 28-day cycle

Investigational medicinal product name	Fulvestrant
Investigational medicinal product code	
Other name	Faslodex
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

500 mg intramuscularly (IM) on Days 1 and 15 of Cycle 1, and then on Day 1 of each subsequent 28 day cycle

Arm title	Arm B (Control): Placebo and Fulvestrant

Arm description:

Placebo: intravenously (IV) on day 1 and 15 of each 28-day cycle
Fulvestrant: (a drug treatment of hormone receptor-positive metastatic breast cancer in post-menopausal women with disease progression following anti-estrogen therapy. It is an estrogen receptor antagonist with no agonist effects, which works both by down-regulating and by degrading the estrogen receptor): 500 mg intramuscularly (IM) on Days 1 and 15 of Cycle 1, and then on Day 1 of each subsequent 28 day cycle

Arm type	Placebo and Fulvestrant
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Solution containing 20 mM histidine, 150 mM sodium chloride, at a pH of 6.5
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Intravenously (IV) on day 1 and 15 of each 28-day cycle

Investigational medicinal product name	Fulvestrant
Investigational medicinal product code	
Other name	Faslodex
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

500 mg intramuscularly (IM) on Days 1 and 15 of Cycle 1, and then on Day 1 of each subsequent 28 day cycle

Number of subjects in period 1	Arm A (Experimental): Seribantumab and Fulvestrant	Arm B (Control): Placebo and Fulvestrant
Started	11	11
Completed	11	11

Baseline characteristics

Reporting groups

Reporting group title	Arm A (Experimental): Seribantumab and Fulvestrant

Reporting group description:

Seribantumab (a human monoclonal antibody that targets ErbB3, a cell surface receptor that is activated by the ligand heregulin. Heregulin-driven ErbB3 signaling has been implicated as a mechanism of tumor growth and resistance to targeted, cytotoxic and anti-endocrine therapies. When used in the combination setting, seribantumab is designed to block ErbB3 signaling in order to enhance the anti-tumor effect of a combination therapy partner): fixed dose of 3000 mg intravenously (IV) on day 1 and 15 of each 28-day cycle
Fulvestrant (a drug treatment of hormone receptor-positive metastatic breast cancer in post-menopausal women with disease progression following anti-estrogen therapy. It is an estrogen receptor antagonist with no agonist effects, which works both by down-regulating and by degrading the estrogen receptor): 500 mg intramuscularly (IM) on Days 1 and 15 of Cycle 1, and then on Day 1 of each subsequent 28 day cycle

Reporting group title	Arm B (Control): Placebo and Fulvestrant

Reporting group description:

Placebo: intravenously (IV) on day 1 and 15 of each 28-day cycle
Fulvestrant: (a drug treatment of hormone receptor-positive metastatic breast cancer in post-menopausal women with disease progression following anti-estrogen therapy. It is an estrogen receptor antagonist with no agonist effects, which works both by down-regulating and by degrading the estrogen receptor): 500 mg intramuscularly (IM) on Days 1 and 15 of Cycle 1, and then on Day 1 of each subsequent 28 day cycle

Reporting group values	Arm A (Experimental): Seribantumab and Fulvestrant	Arm B (Control): Placebo and Fulvestrant	Total
Number of subjects	11	11	22
Age categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	8	7	15
>=65 years	3	4	7
Gender categorical Units: Subjects			
Female	11	11	22
Male	0	0	0
Metastatic burden			
Based upon the population treated, the most important baseline measure was CT scans to determine metastatic burden, as the primary endpoint was investigator assessed PFS. TNM Staging (Tumor size): T1 (T1a,T1b & T1c): 2 cm (3/4 of an inch) or less across. T2: > 2 cm but not more than 5 cm (2 inches) across. T3: > 5 cm across. T4 (T4a,T4b,T4c,T4d): Tumor of any size growing into the chest wall or skin. As a rule, the lower the number, the less the cancer has spread. A higher number, such as stage IV, means cancer has spread more. And within a stage, an earlier letter means a lower stage.			
Units: Subjects			
TNM Stage I	0	1	1
TNM Stage II	0	2	2
TNM Stage IIa	4	0	4
TNM Stage IIb	1	0	1
TNM Stage III	0	2	2
TNM Stage IIIa	1	0	1

TNM Stage IIIc	1	0	1
TNM Stage IV	4	6	10
Heregulin positive status and staining in archival tissue			
Measure Description: Women had to be ≥ HRG 1+ positive in their submitted tumor sample to qualify for the study			
Units: Subjects			
Heregulin positive status and staining in archival	11	11	22

Subject analysis sets

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

Subject analysis set description:

Intent to treat (ITT) population treated up to 150 days

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

Subject analysis set description:

The safety population includes patients receiving at least one dose of study medication. All safety analyses were to be performed on this population.

Reporting group values	Intent to Treat	Safety analysis	
Number of subjects	22	22	
Age categorical Units: Subjects			
<=18 years			
Between 18 and 65 years			
>=65 years			
Gender categorical Units: Subjects			
Female	22	22	
Male	0	0	
Metastatic burden			
Based upon the population treated, the most important baseline measure was CT scans to determine metastatic burden, as the primary endpoint was investigator assessed PFS. TNM Staging (Tumor size): T1 (T1a,T1b & T1c): 2 cm (3/4 of an inch) or less across. T2: > 2 cm but not more than 5 cm (2 inches) across. T3: > 5 cm across. T4 (T4a,T4b,T4c,T4d): Tumor of any size growing into the chest wall or skin. As a rule, the lower the number, the less the cancer has spread. A higher number, such as stage IV, means cancer has spread more. And within a stage, an earlier letter means a lower stage.			
Units: Subjects			
TNM Stage I	1	1	
TNM Stage II	2	2	
TNM Stage IIa	4	4	
TNM Stage IIb	1	1	
TNM Stage III	2	2	
TNM Stage IIIa	1	1	
TNM Stage IIIc	1	1	
TNM Stage IV	10	10	
Heregulin positive status and staining in archival tissue			
Measure Description: Women had to be ≥ HRG 1+ positive in their submitted tumor sample to qualify			

for the study			
Units: Subjects			
Heregulin positive status and staining in archival	22	22	

End points

End points reporting groups

Reporting group title	Arm A (Experimental): Seribantumab and Fulvestrant

Reporting group description:

Seribantumab (a human monoclonal antibody that targets ErbB3, a cell surface receptor that is activated by the ligand heregulin. Heregulin-driven ErbB3 signaling has been implicated as a mechanism of tumor growth and resistance to targeted, cytotoxic and anti-endocrine therapies. When used in the combination setting, seribantumab is designed to block ErbB3 signaling in order to enhance the anti-tumor effect of a combination therapy partner): fixed dose of 3000 mg intravenously (IV) on day 1 and 15 of each 28-day cycle
Fulvestrant (a drug treatment of hormone receptor-positive metastatic breast cancer in post-menopausal women with disease progression following anti-estrogen therapy. It is an estrogen receptor antagonist with no agonist effects, which works both by down-regulating and by degrading the estrogen receptor): 500 mg intramuscularly (IM) on Days 1 and 15 of Cycle 1, and then on Day 1 of each subsequent 28 day cycle

Reporting group title	Arm B (Control): Placebo and Fulvestrant

Reporting group description:

Placebo: intravenously (IV) on day 1 and 15 of each 28-day cycle
Fulvestrant: (a drug treatment of hormone receptor-positive metastatic breast cancer in post-menopausal women with disease progression following anti-estrogen therapy. It is an estrogen receptor antagonist with no agonist effects, which works both by down-regulating and by degrading the estrogen receptor): 500 mg intramuscularly (IM) on Days 1 and 15 of Cycle 1, and then on Day 1 of each subsequent 28 day cycle

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

Subject analysis set description:

Intent to treat (ITT) population treated up to 150 days

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

Subject analysis set description:

The safety population includes patients receiving at least one dose of study medication. All safety analyses were to be performed on this population.

Primary: Progression Free Survival

End point title	Progression Free Survival[1]

End point description:

Progression Free Survival is defined as the time from randomization to the first documented radiographical progression of disease using RECIST v.1.1 of death from any cause, whichever comes first as assessed by the investigator. The tumor assessment (i.e., scan dates) was used for progression/censor date not the date corresponding to the determination of overall response. Progression-free survival time distribution and median survival for each treatment group were analysed using the Kaplan-Meier method.

End point type	Primary

End point timeframe:

Randomization until progression of disease of death due to any cause up to 13 months (the study terminated prematurely). The primary analysis was planned to be initiated when 58 PFS events have occurred

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: Because of the small sample size at the time of the premature study closure, only partial data are summarized in the final tables and listings, and a full clinical study report will not be written. There were no efficacy, pharmacokinetic, or biomarker data feasible for the analysis, and as such, no related analyses were performed.

End point values	Arm A (Experimental) : Seribantumab and Fulvestrant	Arm B (Control): Placebo and Fulvestrant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: participants				
number (not applicable)	1	1		

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 randomization to the date of death from any cause. The study was terminated on 30 Nov 2018. Data represented outcomes up to 150 days of treatment.

End point type	Secondary

End point timeframe:

Randomization until death due to any cause up to 13 months (the study terminated prematurely)

End point values	Arm A (Experimental) : Seribantumab and Fulvestrant	Arm B (Control): Placebo and Fulvestrant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: participants				
number (not applicable)	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate

End point title	Objective Response Rate

End point description:

Objective Response Rate (ORR) is defined as the proportion of patients with a RECIST v1.1 response recorded from randomization until disease progression characterized as either a Complete Response (CR) or Partial Response (PR) relative to the total number of evaluable patients.

End point type	Secondary

End point timeframe:

Randomization through end of study up to 13 months (the study terminated prematurely)

End point values	Arm A (Experimental): Seribantumab and Fulvestrant	Arm B (Control): Placebo and Fulvestrant	Intent to Treat	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	0[2]	0[3]	0[4]	
Units: participants				
number (not applicable)				
Overall Number of Participants Analysed				

Notes:

[2] - All patients analysed had progressive disease. Therefore, they did not meet the criteria for ORR.

[3] - All patients analysed had progressive disease. Therefore, they did not meet the criteria for ORR

[4] - All patients analysed had progressive disease. Therefore, they did not meet the criteria for ORR

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Progression

End point title	Time to Progression

End point description:

Time to Progression (TTP) is defined as the time from the date of randomization to the date of objective tumor progression.

End point type	Secondary

End point timeframe:

Randomization to date of objective tumor progression up to 13 months (the study terminated prematurely)

End point values	Arm A (Experimental): Seribantumab and Fulvestrant	Arm B (Control): Placebo and Fulvestrant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: Days				
median (inter-quartile range (Q1-Q3))				
Time to progression	52 (33.25 to 72.25)	48 (34.50 to 58.50)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participant With Treatment-emergent Adverse Events Reported with the combinations of Seribantumab Plus Fulvestrant versus Fulvestrant Alone

End point title	Number of Participant With Treatment-emergent Adverse Events Reported with the combinations of Seribantumab Plus Fulvestrant versus Fulvestrant Alone

End point description:

Treatment-emergent adverse events (TEAEs) are defined as any event that occurred after the first dose of study drug and was not present prior to study drug administration or worsened in severity after study drug administration.

End point type	Secondary

End point timeframe:

TEAEs were collected through the study completion (30Nov2018), up to 13 months. Frequency and percent summaries were presented for TEAE defined as adverse events that occurs or worsen in severity following the first dose of seribantumab, or fulvestrant.

End point values	Arm A (Experimental) : Seribantumab and Fulvestrant	Arm B (Control): Placebo and Fulvestrant	Safety analysis	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	11	11	22	
Units: Participants				
Patients with any TEAE- Related	7	4	11	
Patients with any TEAE-Serious Adverse event	1	0	1	
NCI-CTCAE Grade 3 or Higher	2	1	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Treatment-emergent Adverse Events Reported with the Combination of Seribantumab Plus Fulvestrant Versus Fulvestrant Alone

End point title	Percentage of Treatment-emergent Adverse Events Reported with the Combination of Seribantumab Plus Fulvestrant Versus Fulvestrant Alone

End point description:

Treatment-emergent adverse events (TEAEs) are defined as any event that occurred after the first dose of study drug and was not present prior to study drug administration or worsened in severity after study drug administration.

End point type	Secondary

End point timeframe:

TEAEs were collected through the study completion (30 Nov 2018), up to 13 months. Frequency and percent summaries were presented for TEAE defined as adverse events that occur or worsen in severity following the first dose of seribantumab, or fulvestrant.

End point values	Arm A (Experimental) : Seribantumab and Fulvestrant	Arm B (Control): Placebo and Fulvestrant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percent				
number (not applicable)				
TEAE-related	63.6	36.4		
TEAE-Serious Adverse event	9.1	0		
NCI-CTCAE Grade 3 or Higher	18.2	9.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic (PK) Profile of Seribantumab When Given in Combination With Furlvestrant and of Fulvestrant When Given in Combination With Seribantumab

End point title	Pharmacokinetic (PK) Profile of Seribantumab When Given in Combination With Furlvestrant and of Fulvestrant When Given in Combination With Seribantumab

End point description:

Pharmacokinetic (PK) evaluation are performed on samples obtained pre-dose on day 1 and 15 of each 28-day cycle to assess pre-treatment trough concentration of MM-121. The maximum observed concentration (Cmax) is presented and calculated using Non compartmental analysis (NCA) . Serum levels of MM-121 are measured at a central lab using an enzyme-linked immunosorbent assay (ELISA).

End point type	Secondary

End point timeframe:

The study terminated prematurely after 13 months. Were to be analysed post-dose on Cycle 1, Week 1 & pre-dose for all subsequent seribantumab infusion until the completion of Cycle 2. Fulvestrant PK sample were to be collected prior to seribantumab dose.

End point values	Arm A (Experimental) : Seribantumab and Fulvestrant	Arm B (Control): Placebo and Fulvestrant	Intent to Treat	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	0[5]	0[6]	0[7]	
Units: participants				
number (not applicable)				

Notes:

[5] - There was no PK data feasible for the analysis, and as such, no related analyses were performed

[6] - There was no PK data feasible for the analysis, and as such, no related analyses were performed

[7] - No data displayed because Outcome Measure has zero total analyzed.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline through to premature study completion up to 13 months (30 Nov 2018).

Adverse event reporting additional description:

The safety population includes patients receiving at least one dose of study medication. All safety analyses were be performed on this population. Safety analyses (AE and laboratory analyses) were performed using the safety population. AE were coded using the latest MedDRA dictionary 21.0. Severity of AE was grade according to the NCI CTCAE v.4.03.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Arm A (Experimental): Seribantumab and Fulvestrant

Reporting group description:

Seribantumab (a human monoclonal antibody that targets ErbB3, a cell surface receptor that is activated by the ligand heregulin. Heregulin-driven ErbB3 signaling has been implicated as a mechanism of tumor growth and resistance to targeted, cytotoxic and anti-endocrine therapies. When used in the combination setting, seribantumab is designed to block ErbB3 signaling in order to enhance the anti-tumor effect of a combination therapy partner): fixed dose of 3000 mg intravenously (IV) on day 1 and 15 of each 28-day cycle

Fulvestrant (a drug treatment of hormone receptor-positive metastatic breast cancer in post-menopausal women with disease progression following anti-estrogen therapy. It is an estrogen receptor antagonist with no agonist effects, which works both by down-regulating and by degrading the estrogen receptor): 500 mg intramuscularly (IM) on Days 1 and 15 of Cycle 1, and then on Day 1 of each subsequent 28 day cycle

Reporting group title	Arm B (Control): Placebo and Fulvestrant

Reporting group description:

Placebo: intravenously (IV) on day 1 and 15 of each 28-day cycle

Fulvestrant: (a drug treatment of hormone receptor-positive metastatic breast cancer in post-menopausal women with disease progression following anti-estrogen therapy. It is an estrogen receptor antagonist with no agonist effects, which works both by down-regulating and by degrading the estrogen receptor): 500 mg intramuscularly (IM) on Days 1 and 15 of Cycle 1, and then on Day 1 of each subsequent 28 day cycle

Serious adverse events	Arm A (Experimental): Seribantumab and Fulvestrant	Arm B (Control): Placebo and Fulvestrant	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Musculoskeletal and connective tissue disorders			
Arthralgia			

subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (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: 0 %

Non-serious adverse events	Arm A (Experimental): Seribantumab and Fulvestrant	Arm B (Control): Placebo and Fulvestrant	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 11 (90.91%)	8 / 11 (72.73%)	
Vascular disorders			
Hot flush			
subjects affected / exposed	2 / 11 (18.18%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Jugular vein thrombosis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 11 (27.27%)	1 / 11 (9.09%)	
occurrences (all)	3	1	
Fatigue			
subjects affected / exposed	2 / 11 (18.18%)	1 / 11 (9.09%)	
occurrences (all)	2	1	
Chest discomfort			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Influenza like likeness			

subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Injection site pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Injection site reaction			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Malaise			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Vulvovaginal pruritus			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 11 (18.18%)	1 / 11 (9.09%)	
occurrences (all)	2	1	
Cough			
subjects affected / exposed	1 / 11 (9.09%)	1 / 11 (9.09%)	
occurrences (all)	1	1	
Epistaxis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Nasal dryness			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Pleural effusion			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Psychiatric disorders			

Depression			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Irritability			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Blood bilirubin increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
White blood cell count decreased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	2 / 11 (18.18%)	1 / 11 (9.09%)	
occurrences (all)	2	1	
Headache			
subjects affected / exposed	2 / 11 (18.18%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Hypoaesthesia			
subjects affected / exposed	1 / 11 (9.09%)	1 / 11 (9.09%)	
occurrences (all)	1	1	

Paraesthesia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 11 (18.18%)	1 / 11 (9.09%)	
occurrences (all)	2	1	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Dry eye			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Eye allergy			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Lacrimation increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Vision blurred			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	7 / 11 (63.64%)	3 / 11 (27.27%)	
occurrences (all)	7	3	
Nausea			
subjects affected / exposed	2 / 11 (18.18%)	3 / 11 (27.27%)	
occurrences (all)	2	3	
Dyspepsia			
subjects affected / exposed	3 / 11 (27.27%)	0 / 11 (0.00%)	
occurrences (all)	3	0	
Oral pain			
subjects affected / exposed	2 / 11 (18.18%)	1 / 11 (9.09%)	
occurrences (all)	2	1	

Abdominal pain			
subjects affected / exposed	0 / 11 (0.00%)	2 / 11 (18.18%)	
occurrences (all)	0	2	
Stomatitis			
subjects affected / exposed	2 / 11 (18.18%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Constipation			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Dry mouth			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Dysphagia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Faeces soft			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Odynophagia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Salivary hypersecretion			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Hepatobiliary disorders			
Hepatomegaly			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	2 / 11 (18.18%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Alopecia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Dry skin			

subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Pain of skin			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Rash maculo-papular			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 11 (9.09%)	1 / 11 (9.09%)	
occurrences (all)	1	1	
Urine odour abnormal			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 11 (18.18%)	1 / 11 (9.09%)	
occurrences (all)	2	1	
Back pain			
subjects affected / exposed	1 / 11 (9.09%)	1 / 11 (9.09%)	
occurrences (all)	1	1	
Bone pain			
subjects affected / exposed	1 / 11 (9.09%)	1 / 11 (9.09%)	
occurrences (all)	1	1	
Musculoskeletal pain			
subjects affected / exposed	2 / 11 (18.18%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Flank pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Groin pain			

subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Joint swelling			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Muscle spasms			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Neck pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Pain in extremity			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Pain in jaw			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	2 / 11 (18.18%)	1 / 11 (9.09%)	
occurrences (all)	2	1	
Upper respiratory tract infection			
subjects affected / exposed	1 / 11 (9.09%)	1 / 11 (9.09%)	
occurrences (all)	1	1	
Fungal infection			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	3 / 11 (27.27%)	5 / 11 (45.45%)	
occurrences (all)	3	5	
Hypokalaemia			
subjects affected / exposed	1 / 11 (9.09%)	1 / 11 (9.09%)	
occurrences (all)	1	1	
Hypercalcaemia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Hyperuricaemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Hypocalcaemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Hypomagnesaemia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Hypochloraemia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 April 2017	Amendment 1.1: The rationale for making this change from a Phase 3 potential registration study to a Phase 2 proof of concept study, that it is not intended to support a marketing application, follows from a corporate project portfolio review at Merrimack.
28 April 2017	Amendment 1.2: Minor administrative changes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Sponsor (Merrimack Pharmaceuticals, INC.) terminated the trial early due to business decision.

Notes: