Clinical trial results:
Phase II, open-label, non-randomized study of nab-paclitaxel for the neoadjuvant treatment of patients with stage II and III luminal breast cancer.

Summary

EudraCT number	2011-004476-10
Trial protocol	ES
Global end of trial date	27 May 2018

Results information

Result version number	v1 (current)
This version publication date	17 October 2020
First version publication date	17 October 2020

Trial information

Trial identification

Sponsor protocol code	GEICAM/2011-02

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01565499
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GEICAM (FUNDACIÓN GRUPO ESPAÑOL DE INVESTIGACIÓN EN CÁNCER DE MAMA)
Sponsor organisation address	Avenida de los Pirineos 7, San Sebastián de los Reyes / Madrid, Spain, 28703
Public contact	GEICAM, GEICAM, +34 916592870, inicio_ensayos@geicam.org
Scientific contact	GEICAM, GEICAM, +34 916592870, inicio_ensayos@geicam.org

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	17 October 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 May 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the percentage of patients with poor response [residual cancer burden III (RCB-III) rate] in contrast to good response [residual cancer burden 0/I RCB-0/1] measured by the Symmans criteria [20] at surgery, in patients with stage II-III luminal breast cancer treated with neoadjuvant nab-paclitaxel.

Protection of trial subjects:

Not applicable. It was not necessary to applied extra measures for protection of the subjects out of the good clinical practice environment.

Background therapy:

The use of chemotherapy in the neoadjuvant setting is a good treatment choice for either premenopausal ER positive patients, or patients with high Ki-67.
nab-Paclitaxel is a novel formulation of paclitaxel that consists of nanometer-range particles of paclitaxel bound of human serum albumin. nab-Paclitaxel exploits the role of of albumin as the natural carrier of hidrofobic molecules in human to increase paclitaxel delivery to tumor cells, eliminating the need for solvents.
nab-Paclitaxel (every three weeks) showed a significant higher ORR and longer TTP than standard paclitaxel (every three weeks) in a phase III study in metastatic breast cancer. Weekly nab-Paclitaxel also demonstrated a superior efficacy and safety than every three weeks docetaxel in a randomized phase II study. The nab-paclitaxel weekly dose of 150 mg/m2 appeared to be the most effective.
This study proposes evaluating the activity and safety profile of weekly nab-paclitaxel administered at a dose of 150 mg/m2 (on days 1,8 and 15 every four weeks) for 4 cycles cycles as the neoadjuvant treatment of women with positive estrogen receptors and negative HER2, amenable to receive chemotherapy.
Likewise, biomarkers will be investigated for the purpose of aiding and improving the understanding of the efficacy, safety and mechanism of action of nab-paclitaxel in these patients.

Evidence for comparator: -

Actual start date of recruitment	17 April 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 81
Worldwide total number of subjects	81
EEA total number of subjects	81

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)	73
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Between April 2012 and January 2013, 83 patients were registered in 15 Spanish sites. Two of them never received treatment
and were excluded from the analysis, so the number of subjects enrolled is 81.

Pre-assignment

Screening details:

Between April 2012 and January 2013, 83 patients were registered in 15 Spanish sites. Two of them never received treatment
and were excluded from the analysis, so the number of subjects enrolled is 81.

Period 1

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

Arms

Arm title	Nab-Paclitaxel

Arm description:

The patients were included to receive 3 weekly nab-paclitaxel doses of 150 mg/m2 with one week of rest for 4 cycles.
There are 2 patients that have not received any cycle and they are excluded of analysis by Intention to Treat (ITT) criterium: One does not receive any cycle, she ended treatment by investigator´s criterium and the other withdraws informed consent before starting the treatment.

Arm type	Experimental
Investigational medicinal product name	Nab-paclitaxel
Investigational medicinal product code	
Other name	Abraxane
Pharmaceutical forms	Concentrate and solvent for suspension for injection
Routes of administration	Intravenous use

Dosage and administration details:

Treatment Administered: nab-Paclitaxel: administered at a dose of 150 mg/m2 as a 30 minutes intravenous infusion on days 1, 8 and 15 in cycles of 28 days for 4 cycles.

Number of subjects in period 1	Nab-Paclitaxel
Started	81
Completed	75
Not completed	6
Consent withdrawn by subject	1
Adverse event, non-fatal	5

Baseline characteristics

Reporting groups	
Reporting group title	Nab-Paclitaxel
Reporting group description:	
The patients were included to receive 3 weekly nab-paclitaxel doses of 150 mg/m2 with one week of rest for 4 cycles. There are 2 patients that have not received any cycle and they are excluded of analysis by Intention to Treat (ITT) criterium: One does not receive any cycle, she ended treatment by investigator´s criterium and the other withdraws informed consent before starting the treatment.	

Reporting group values	Nab-Paclitaxel	Total	
Number of subjects	81	81	
Age categorical Units: Subjects			
Adults (18-64 years)	73	73	
From 65-84 years	8	8	
Age continuous Units: years			
median	47		
full range (min-max)	28 to 75	-	
Gender categorical Units: Subjects			
Female	81	81	
Male	0	0	
Race Units: Subjects			
Caucasian	79	79	
Hispanic	2	2	
Menopausal Status Units: Subjects			
Postmenopausal	29	29	
Premenopausal	52	52	
Hormonal status Units: Subjects			
Estrogen Receptor (ER) (+) and Progesterone R (+)	62	62	
ER (+) and Progesterone R (-)	17	17	
ER (+) and Progesterone R (Not available)	2	2	
Clinical Stage			
Measure Description: According to American Joint Committee on Cancer (AJCC) 2002: • Stage (S) I: tumour <2 centimetres (cm) • S II: S IIA: cancer spread to movable ipsilateral axillary (MIA) Lymph Nodes (LN). tumor <2 cm and spread to MIA LN tumor >2 cm but >5 cm S IIB: tumor >2 cm but <5 cm and spread to MIA LN tumor >5 cm • S III: S IIIA: cancer spread to ipsilateral axillary LN fixed or matted S IIIB: tumor spread to the chest wall or caused swelling or ulceration of the breast or is diagnosed as inflammatory breast cancer. S IIIC: metastases in ipsilateral infraclavicular LN.			
Units: Subjects			

Stage I	4	4	
Stage II	56	56	
Stage III	18	18	
Unknown	3	3	
Histopathologic Grade			
Cancer cells are given a Grade (G) when they are removed from the breast and checked under a microscope. The G is based on how much the cancer cells look like normal cells. • G1 or well differentiated (score 3, 4, or 5): cells are slower-growing, and look more like normal breast tissue. • G2 or moderately differentiated (score 6, 7): cells are growing at a speed of and look like cells somewhere between G1 and 3. • G3 or poorly differentiated (score 8, 9): cells look very different from normal and will probably grow and spread faster.			
Units: Subjects			
Grade 1	9	9	
Grade 2	39	39	
Grade 3	26	26	
Unknown	7	7	
Breast Surgery Planned Units: Subjects			
Mastectomy	50	50	
Quadrantectomy	17	17	
Lumpectomy	10	10	
Not available	4	4	
Eastern Cooperative Oncology Group (ECOG) status Units: Subjects			
ECOG 0	79	79	
ECOG 1	2	2	
Histopathologic Type Units: Subjects			
Infiltrating Ductal Carcinoma	74	74	
Infiltrating Lobular Carcinoma	7	7	

End points

End points reporting groups

Reporting group title	Nab-Paclitaxel

Reporting group description:

The patients were included to receive 3 weekly nab-paclitaxel doses of 150 mg/m2 with one week of rest for 4 cycles.
There are 2 patients that have not received any cycle and they are excluded of analysis by Intention to Treat (ITT) criterium: One does not receive any cycle, she ended treatment by investigator´s criterium and the other withdraws informed consent before starting the treatment.

Primary: The Residual Cancer Burden Grade III (RCB-III)

End point title	The Residual Cancer Burden Grade III (RCB-III)[1]

End point description:

The estimate of the RCB-III was calculated as follows: Overall Response Rate = Number of patients with RCB-III / Intent to treat (ITT) population

End point type	Primary

End point timeframe:

After surgery, up to 4 months

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The estimate of the RCB-III was calculated as follows: Overall Response Rate = Number of patients with RCB-III / Intent to treat (ITT) population

End point values	Nab-Paclitaxel			
Subject group type	Reporting group			
Number of subjects analysed	81			
Units: Count of Participants	23			

Statistical analyses

No statistical analyses for this end point

Secondary: Pathologic Complete Response (pCR) Rate

End point title	Pathologic Complete Response (pCR) Rate

End point description:

The estimate of the pCR rate was calculated as follows by central laboratory: pCR Rate = Number of patients with pCR / ITT population.

End point type	Secondary

End point timeframe:

After surgery, up to 4 months

End point values	Nab-Paclitaxel			
Subject group type	Reporting group			
Number of subjects analysed	81			
Units: Count of Participants	6			

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR) by Magnetic Resonance Imaging (MRI)

End point title	Objective Response Rate (ORR) by Magnetic Resonance Imaging (MRI)

End point description:

The estimate of the ORR was determined according to RECIST 1.1 and measured by MRI and mammogram in patients treated with this regimen. ORR was calculated as follows: Overall Response Rate = Number of Complete Responses (CRs), Partial Responses (PRs) / ITT population

End point type	Secondary

End point timeframe:

After surgery, up to 4 months

End point values	Nab-Paclitaxel			
Subject group type	Reporting group			
Number of subjects analysed	81			
Units: Count of participants	62			

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR) by Mammogram

End point title	Objective Response Rate (ORR) by Mammogram

End point description:

The ORR was reported including a 95% confidence interval. The estimate of the ORR was determined according to RECIST 1.1 and measured by MRI and mammogram in patients treated with this regimen. ORR was calculated as follows: Overall Response Rate = Number of CRs, PRs / ITT population

End point type	Secondary

End point timeframe:

After surgery, up to 4 months

End point values	Nab-Paclitaxel			
Subject group type	Reporting group			
Number of subjects analysed	81			
Units: Count of Participants	49			

Statistical analyses

No statistical analyses for this end point

Secondary: Invasive Disease Free Survival (IDFS)

End point title	Invasive Disease Free Survival (IDFS)

End point description:

IDFS was defined as the time (days) from the date of randomization until the date of objective recurrent disease (local, regional or distant), second primary invasive malignancy (breast or non-breast) or death from any cause. For patients not known to have died as of the data cut-off date and who do not have recurrent disease or second primary tumor, invasive disease-free survival will be censored at the last contact date. Ductal carcinoma in-situ (DCIS) will not be considered an event for the purpose of this analysis.

End point type	Secondary

End point timeframe:

After surgery, up to 4 months

End point values	Nab-Paclitaxel			
Subject group type	Reporting group			
Number of subjects analysed	81			
Units: Years				
median (standard deviation)	4.89 (± 1.10)			

Attachments (see zip file)	Invasive Disease Free Survival/2011-02 IDFS.docx

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of Conversion to Breast Conserving Surgery (BCS)

End point title	Rate of Conversion to Breast Conserving Surgery (BCS)

End point description:

The estimate of the rate of conversion to BCS was calculated as follows: BCS rate = Number of patients with BCS / Number of patients with initially planned mastectomy.

End point type	Secondary

End point timeframe:

After surgery, up to 4 months

End point values	Nab-Paclitaxel			
Subject group type	Reporting group			
Number of subjects analysed	50			
Units: Patients with BCS	20			

Statistical analyses

No statistical analyses for this end point

Secondary: Ki67 in Pre-treatment Tumor Samples as Tumor Predictive Marker of Nab-paclitaxel Response

End point title	Ki67 in Pre-treatment Tumor Samples as Tumor Predictive Marker of Nab-paclitaxel Response

End point description:

Ki67 was analysed by immunohistochemistry following the American Society of Clinical Oncology and the College of American Pathologists guidelines. The cut-off considered for Ki67 expression was 20% of positively stained tumor cells.

End point type	Secondary

End point timeframe:

Baseline: in Pre-treatment Tumor Samples

End point values	Nab-Paclitaxel			
Subject group type	Reporting group			
Number of subjects analysed	72			
Units: Participants				
number (not applicable)				
≥ 20 %	40			
< 20 %	32			

Statistical analyses

No statistical analyses for this end point

Secondary: Caveolin-1 in Pre-treatment Tumor Samples as Tumor Predictive Marker of Nab-paclitaxel Response

End point title	Caveolin-1 in Pre-treatment Tumor Samples as Tumor Predictive Marker of Nab-paclitaxel Response

End point description:

Caveolin (Cav)-1 was evaluated in the stroma and its expression was categorized in low, moderate, or high (tertile). The high expression of Cav-1 was considered as positive.

End point type	Secondary

End point timeframe:

Baseline: Pre-treatment Tumor Samples

End point values	Nab-Paclitaxel			
Subject group type	Reporting group			
Number of subjects analysed	72			
Units: Participants				
number (not applicable)				
Positive	19			
Negative	53			

Statistical analyses

No statistical analyses for this end point

Secondary: Secreted Protein, Acidic, Cysteine-rich (SPARC) in Pre-treatment Tumor Samples as Tumor Predictive Marker of Nab-paclitaxel Response

End point title	Secreted Protein, Acidic, Cysteine-rich (SPARC) in Pre-treatment Tumor Samples as Tumor Predictive Marker of Nab-paclitaxel Response

End point description:

SPARC was evaluated for both tumor and stroma. Its expression was categorized as negative when the intensity was absent-to-weak (1), or moderate (11)-to-strong (111) with a proportion of stained cells <10%. Immunolabeling was positive if the intensity was moderate (11)-to-strong (111) and the extent of staining was 10%.

End point type	Secondary

End point timeframe:

Baseline: Pre-treatment Tumor Samples

End point values	Nab-Paclitaxel			
Subject group type	Reporting group			
Number of subjects analysed	72			
Units: Participants				
number (not applicable)				
Positive	7			
Negative	65			

Statistical analyses

No statistical analyses for this end point

Secondary: Molecular Tumor Subtypes According to St. Gallen Criteria 2013 in Pre-

treatment Tumor Samples as Predictive Marker of Nab-paclitaxel Response

End point title	Molecular Tumor Subtypes According to St. Gallen Criteria 2013 in Pre-treatment Tumor Samples as Predictive Marker of Nab-paclitaxel Response

End point description:

Molecular subtypes were classified according to St. Gallen criteria 2013 and Prat et al. into Luminal A (ER+, PgR >20%, HER2-, Ki67 <14%), Luminal B1 (ER+, HER2-, PgR >20% and/or Ki67 <14%), Luminal B2 (ER+, HER2+, any PgR, any Ki67), TN (ER-, PgR-, HER2-), and HER2-enriched (ER-, PgR-, HER2+) subtypes.

End point type	Secondary

End point timeframe:

Baseline: Pre-treatment Tumor Samples

End point values	Nab-Paclitaxel			
Subject group type	Reporting group			
Number of subjects analysed	72			
Units: Participants				
number (not applicable)				
Luminal A	19			
Luminal B1	53			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events (AEs) and Serious Adverse Events (SAEs) were recorded from the date informed consent was signed, during treatment period, and for up 30 days after the last dose of each patient. Thereafter all study drug-related SAEs were reported.

Assessment type	Systematic

Dictionary used

Dictionary name	NCI-CTC
Dictionary version	4.03

Reporting groups

Reporting group title	Nab-Paclitaxel

Reporting group description: -

Serious adverse events	Nab-Paclitaxel		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 81 (7.41%)		
number of deaths (all causes)	4		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Multiple Sclerosis Relapse			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neurotoxicity			
subjects affected / exposed	2 / 81 (2.47%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Community-acquired pneumonia			

subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Local Infection Reservoir Area			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Nab-Paclitaxel		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	81 / 81 (100.00%)		
Investigations			
NEUTROPHIL COUNT DECREASED grade 3			
subjects affected / exposed	10 / 81 (12.35%)		
occurrences (all)	10		
NEUTROPHIL COUNT DECREASED grade 2			
subjects affected / exposed	22 / 81 (27.16%)		
occurrences (all)	22		
NEUTROPHIL COUNT DECREASED grade 1			
subjects affected / exposed	21 / 81 (25.93%)		
occurrences (all)	21		
WHITE BLOOD CELL DECREASED grade 2			
subjects affected / exposed	21 / 81 (25.93%)		
occurrences (all)	21		
WHITE BLOOD CELL DECREASED grade 1			
subjects affected / exposed	29 / 81 (35.80%)		
occurrences (all)	29		
ALANINE AMINOTRANSFERASE INCREASED grade 1			
subjects affected / exposed	32 / 81 (39.51%)		
occurrences (all)	32		

ALKALINE PHOSPHATASE INCREASED grade 1			
subjects affected / exposed	8 / 81 (9.88%)		
occurrences (all)	8		
ASPARTATE AMINOTRANSFERASE INCREASED grade 1			
subjects affected / exposed	14 / 81 (17.28%)		
occurrences (all)	14		
CHOLESTEROL HIGH grade 1			
subjects affected / exposed	5 / 81 (6.17%)		
occurrences (all)	5		
HYPERCALCEMIA grade 1			
subjects affected / exposed	9 / 81 (11.11%)		
occurrences (all)	9		
HYPERGLYCEMIA grade 1			
subjects affected / exposed	18 / 81 (22.22%)		
occurrences (all)	18		
Vascular disorders			
HYPERTENSION grade 3			
subjects affected / exposed	6 / 81 (7.41%)		
occurrences (all)	6		
HYPERTENSION grade 2			
subjects affected / exposed	15 / 81 (18.52%)		
occurrences (all)	15		
HYPERTENSION grade 1			
subjects affected / exposed	6 / 81 (7.41%)		
occurrences (all)	6		
HOT FLASHES grade 1			
subjects affected / exposed	7 / 81 (8.64%)		
occurrences (all)	7		
Nervous system disorders			
PERIPHERAL SENSORY NEUROPATHY grade 2			
subjects affected / exposed	22 / 81 (27.16%)		
occurrences (all)	22		
PERIPHERAL SENSORY NEUROPATHY grade 1			

subjects affected / exposed	40 / 81 (49.38%)		
occurrences (all)	40		
DIZZINESS grade 1			
subjects affected / exposed	8 / 81 (9.88%)		
occurrences (all)	8		
DYSGEUSIA grade 1			
subjects affected / exposed	8 / 81 (9.88%)		
occurrences (all)	8		
HEADACHE grade 1			
subjects affected / exposed	9 / 81 (11.11%)		
occurrences (all)	9		
Blood and lymphatic system disorders			
ANEMIA grade 2			
subjects affected / exposed	6 / 81 (7.41%)		
occurrences (all)	6		
ANEMIA grade 1			
subjects affected / exposed	58 / 81 (71.60%)		
occurrences (all)	58		
ERITROCYTES DECREASE grade 1			
subjects affected / exposed	10 / 81 (12.35%)		
occurrences (all)	10		
General disorders and administration site conditions			
FATIGUE grade 2			
subjects affected / exposed	20 / 81 (24.69%)		
occurrences (all)	20		
FATIGUE grade 1			
subjects affected / exposed	38 / 81 (46.91%)		
occurrences (all)	38		
EDEMA LIMBS grade 1			
subjects affected / exposed	5 / 81 (6.17%)		
occurrences (all)	5		
FEVER grade 1			
subjects affected / exposed	6 / 81 (7.41%)		
occurrences (all)	6		
PAIN IN EXTREMITY grade 1			

subjects affected / exposed occurrences (all)	6 / 81 (7.41%) 6		
Gastrointestinal disorders CONSTIPATION grade 2 subjects affected / exposed occurrences (all) CONSTIPATION grade 1 subjects affected / exposed occurrences (all) DIARRHEA grade 2 subjects affected / exposed occurrences (all) DIARRHEA grade 1 subjects affected / exposed occurrences (all) MUCOSITIS ORAL grade 1 subjects affected / exposed occurrences (all) NAUSEA grade 1 subjects affected / exposed occurrences (all) VOMITING grade 1 subjects affected / exposed occurrences (all)	 5 / 81 (6.17%) 5 8 / 81 (9.88%) 8 5 / 81 (6.17%) 5 23 / 81 (28.40%) 23 13 / 81 (16.05%) 13 23 / 81 (28.40%) 23 6 / 81 (7.41%) 6		
Reproductive system and breast disorders IRREGULAR MENSTRUATION grade 2 subjects affected / exposed occurrences (all) BREAST PAIN grade 1 subjects affected / exposed occurrences (all)	 9 / 81 (11.11%) 9 5 / 81 (6.17%) 5		
Skin and subcutaneous tissue disorders ALOPECIA grade 2 subjects affected / exposed occurrences (all) ALOPECIA grade 1	 54 / 81 (66.67%) 54		

subjects affected / exposed	12 / 81 (14.81%)		
occurrences (all)	12		
NAIL LOSS grade 2			
subjects affected / exposed	6 / 81 (7.41%)		
occurrences (all)	6		
NAIL LOSS grade 1			
subjects affected / exposed	5 / 81 (6.17%)		
occurrences (all)	5		
PRURITUS grade 1			
subjects affected / exposed	9 / 81 (11.11%)		
occurrences (all)	9		
NAIL CHANGES grade 1			
subjects affected / exposed	14 / 81 (17.28%)		
occurrences (all)	14		
RASH grade 1			
subjects affected / exposed	8 / 81 (9.88%)		
occurrences (all)	8		
Psychiatric disorders			
DEPRESSION grade 1			
subjects affected / exposed	5 / 81 (6.17%)		
occurrences (all)	5		
INSOMNIA grade 1			
subjects affected / exposed	9 / 81 (11.11%)		
occurrences (all)	9		
Musculoskeletal and connective tissue disorders			
ARTHRALGIA grade 2			
subjects affected / exposed	7 / 81 (8.64%)		
occurrences (all)	7		
ARTHRALGIA grade 1			
subjects affected / exposed	9 / 81 (11.11%)		
occurrences (all)	9		
MYALGIA grade 2			
subjects affected / exposed	9 / 81 (11.11%)		
occurrences (all)	9		
MYALGIA grade 1			

subjects affected / exposed occurrences (all) BONE PAIN grade 1 subjects affected / exposed occurrences (all)	15 / 81 (18.52%) 15 7 / 81 (8.64%) 7		
Infections and infestations UPPER RESPIRATORY INFECTION grade 2 subjects affected / exposed occurrences (all)	 6 / 81 (7.41%) 6		
Metabolism and nutrition disorders ANOREXIA grade 1 subjects affected / exposed occurrences (all)	 7 / 81 (8.64%) 7		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/28701571