Clinical trial results:
A Phase 3 Open-Label, Randomized, Multicenter Study of NKTR-102 versus Treatment of Physician's Choice (TPC) in Patients with Metastatic Breast Cancer Who Have Stable Brain Metastases and Have Been Previously Treated with an Anthracycline, a Taxane, and Capecitabine

Summary

EudraCT number	2016-002453-38
Trial protocol	GB ES CZ BE PT FR HU IT
Global end of trial date	06 November 2019

Results information

Result version number	v1 (current)
This version publication date	05 August 2021
First version publication date	05 August 2021

Trial information

Trial identification

Sponsor protocol code	15-102-14

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02915744
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Nektar Therapeutics
Sponsor organisation address	455 Mission Bay Blvd South, San Francisco, United States, 94158
Public contact	Medical Affairs, Nektar Therapeutics, 855 482-8676, medicalaffairs@nektar.com
Scientific contact	Medical Affairs, Nektar Therapeutics, 855 482-8676, medicalaffairs@nektar.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 July 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 November 2019
Global end of trial reached?	Yes
Global end of trial date	06 November 2019
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To compare overall survival (OS) of patients who receive 145 mg/m2 NKTR-102 given once every 21 days (q21d) with OS of patients who receive Treatment of Physician's Choice (TPC) selected from the following list of 7 single-agent intravenous (IV) therapies: eribulin, ixabepilone, vinorelbine, gemcitabine, paclitaxel, docetaxel, or nab-paclitaxel. TPC drugs will be administered per the standard of care.

Protection of trial subjects:

Written informed consent was obtained from patients at the Screening Visit prior to performance of any study-specific tests or evaluations. The Investigator, or a person designated by the Investigator, explained to each patient or the patient's legally authorized representative (LAR) the nature of the study, its purpose, the procedures involved, the expected duration, the potential risks and benefits involved, and any discomfort participation in the study may entail. Each patient or the patient's LAR was informed that participation in the study was voluntary and that the patient would be able to withdraw from the study at any time, and that withdrawal of consent would not affect the patient's subsequent medical treatment or relationship with the treating physician.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 March 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	Portugal: 6
Country: Number of subjects enrolled	Spain: 21
Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	Belgium: 17
Country: Number of subjects enrolled	France: 16
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	United States: 85
Country: Number of subjects enrolled	Australia: 13
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Israel: 7
Worldwide total number of subjects	178
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)	149
From 65 to 84 years	29
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Eligibility to the study was inclusive of patients with breast cancer brain metastases and any breast cancer tumor subtype.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	NKTR-102

Arm description:

NKTR-102 will be administered at a dose level of 145 mg/m2 on a q21d schedule as a 90-minute intravenous (IV) infusion on Day 1 of each treatment cycle.

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

Dosage and administration details:

NKTR-102 will be administered at a dose level of 145 mg/m2 on a q21d schedule as a 90-minute intravenous (IV) infusion on Day 1 of each treatment cycle.

Arm title	Treatment of Physician's Choice (TPC)

Arm description:

TPC will be administered per standard of care. Patients randomized to TPC will receive single-agent IV chemotherapy, limited to choice of one of the following 7 agents: eribulin, ixabepilone, vinorelbine, gemcitabine, paclitaxel, docetaxel, or nab-paclitaxel.

Arm type	Active comparator
Investigational medicinal product name	Eribulin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Give specified dose on specified days

Investigational medicinal product name	Ixabepilone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Give specified dose on specified days

Investigational medicinal product name	Vinorelbine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: Give specified dose on specified days	
Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: Give specified dose on specified days	
Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Solution for infusion
Dosage and administration details: Give specified dose on specified days	
Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: Give specified dose on specified days	
Investigational medicinal product name	Nab-paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: Give specified dose on specified days	

Number of subjects in period 1	NKTR-102	Treatment of Physician's Choice (TPC)
Started	92	86
Completed	13	9
Not completed	79	77
Adverse event, serious fatal	3	2
Consent withdrawn by subject	4	14
Physician decision	8	12
Adverse event, non-fatal	11	3
Lost to follow-up	-	1

Lack of efficacy	53	45

Baseline characteristics

Reporting groups	
Reporting group title	NKTR-102
Reporting group description:	
NKTR-102 will be administered at a dose level of 145 mg/m2 on a q21d schedule as a 90-minute intravenous (IV) infusion on Day 1 of each treatment cycle.	
Reporting group title	Treatment of Physician's Choice (TPC)
Reporting group description:	
TPC will be administered per standard of care. Patients randomized to TPC will receive single-agent IV chemotherapy, limited to choice of one of the following 7 agents: eribulin, ixabepilone, vinorelbine, gemcitabine, paclitaxel, docetaxel, or nab-paclitaxel.	

Reporting group values	NKTR-102	Treatment of Physician's Choice (TPC)	Total
Number of subjects	92	86	178
Age categorical Units: Subjects			
Adults (18-64 years)	74	75	149
From 65-84 years	18	11	29
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	54.7	51.9	
standard deviation	± 10.13	± 10.50	-
Gender categorical Units: Subjects			
Female	92	86	178
Male	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	6	8
Not Hispanic or Latino	69	60	129
Unknown or Not Reported	21	20	41
ECOG			
Measure Description: Grade - ECOG Performance Status 0 - Fully active, able to carry on all pre-disease performance without restriction 1 - Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work			
Units: Subjects			
Score of 0	25	25	50
Score of 1	67	61	128
Reproductive Status Units: Subjects			
Of Child-Bearing Potential	16	13	29
Surgically Sterile	11	14	25
Post-Menopausal	65	55	120
Other	0	4	4
Missing	0	0	0
Pregnancy Test at Screening			

Units: Subjects			
Positive	1	1	2
Negative	22	24	46
Borderline	6	1	7
Not Performed	63	60	123
Breast Cancer Stage at Initial Diagnosis Units: Subjects			
Stage I	5	10	15
Stage II	41	29	70
Stage III	22	17	39
Stage IV	10	16	26
Unknown	14	14	28
Cancer History at Initial Diagnosis Units: Subjects			
Invasive Ductal Carcinoma	80	77	157
Invasive Lobular Carcinoma	6	1	7
Other	6	8	14
Estrogen Receptor Status at Initial Diagnosis Units: Subjects			
ER Positive	52	49	101
ER Negative	40	34	74
Unknown	0	3	3
Progesterone Receptor Status at Initial Diagnosis Units: Subjects			
PgR Positive	40	42	82
PgR Negative	50	41	91
Unknown	2	3	5
HER2 Receptor Status at Initial Diagnosis Units: Subjects			
HER2 Positive	15	14	29
HER2 Negative	76	66	142
Unknown	1	6	7
Estrogen Receptor Status at Last Biopsy Units: Subjects			
ER Positive	47	48	95
ER Negative	38	36	74
Unknown	7	2	9
Progesterone Receptor Status at Last Biopsy Units: Subjects			
PgR Positive	32	31	63
PgR Negative	51	52	103
Unknown	9	3	12
HER2 Receptor Status at Last Biopsy Units: Subjects			
HER2 Positive	12	13	25
HER2 Negative	74	69	143
Unknown	6	4	10
Estrogen Receptor/Progesterone Receptor Status at Last Biopsy			

Units: Subjects			
ER/PgR Positive	49	49	98
ER/PgR Negative	36	35	71
Unknown	7	2	9
Race			
Units: Subjects			
White	66	57	123
Black or African-American	3	5	8
Asian	3	6	9
American Indian or Alaska Native	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Other	0	0	0
Not Reported	20	18	38
Missing	0	0	0
Height			
Units: centimeters			
arithmetic mean	162.7	162.1	
standard deviation	± 6.67	± 7.73	-
Weight			
Units: kilograms			
arithmetic mean	67.16	65.97	
standard deviation	± 17.468	± 15.561	-
Time since Initial Breast Cancer Diagnosis			
Units: Years			
arithmetic mean	8.094	6.950	
standard deviation	± 5.17	± 5.0941	-
Time Since Initial Brain Metastasis Diagnosis			
Units: years			
arithmetic mean	1.137	1.194	
standard deviation	± 1.1061	± 1.1748	-

End points

End points reporting groups

Reporting group title	NKTR-102

Reporting group description:

NKTR-102 will be administered at a dose level of 145 mg/m2 on a q21d schedule as a 90-minute intravenous (IV) infusion on Day 1 of each treatment cycle.

Reporting group title	Treatment of Physician's Choice (TPC)

Reporting group description:

TPC will be administered per standard of care. Patients randomized to TPC will receive single-agent IV chemotherapy, limited to choice of one of the following 7 agents: eribulin, ixabepilone, vinorelbine, gemcitabine, paclitaxel, docetaxel, or nab-paclitaxel.

Subject analysis set title	Subject Analysis Set
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All patients who were randomized in the study were included in the ITT population.

Primary: Overall Survival (OS) of Patients

End point title	Overall Survival (OS) of Patients

End point description:

To compare Overall Survival (OS) of patients who receive 145 mg/m2 NKTR-102 given once every 21 days (q21d) with OS of patients who receive Treatment of Physician's Choice (TPC). Overall survival is defined as the time from the date of randomization to the date of death from any cause. Patients will be followed until their date of death or until final database closure. Patients who are lost-to-follow-up or are alive at the time of analysis will be censored at the time they were last known to be alive or at the date of event cut-off for OS analysis.

End point type	Primary

End point timeframe:

Within 3 years from study start

End point values	NKTR-102	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	92	86		
Units: Months				
median (confidence interval 95%)	7.8 (6.1 to 10.2)	7.5 (5.8 to 10.4)		

Statistical analyses

Statistical analysis title	Primary Endpoint Analysis

Statistical analysis description:

The primary analysis of OS was the CHW test with pre-specified weights (Cui, Hung, Wang, 1999). The conventional test with equal weights for every patient was conducted as a sensitivity analysis. The median survival times and their 95% confidence intervals (CIs) as well as survival curves were estimated using the Kaplan-Meier method and were summarized by treatment group. The 2-sided significance level for superiority at final analysis of OS was 0.0499.

Comparison groups	NKTR-102 v Treatment of Physician's Choice (TPC)

Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	≤ 0.0499
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.901
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.612
upper limit	1.326
Variability estimate	Standard deviation

Notes:

[1] - At final analysis, the primary analysis of OS for statistical significance claim will be based on the CHW version of the logrank test statistic with weights (Cui, Hung, & Wang, 1999). Based on the correlation between interim and final CHW test statistic, statistical significance can be claimed if the two-sided p-value for CHW test statistic is no greater than 0.0499. The conventional logrank test with equal weights for every patient will be conducted as a sensitivity analysis.

Secondary: Progression-Free Survival (Outside the Central Nervous System)

End point title	Progression-Free Survival (Outside the Central Nervous System)

End point description:

Progression-Free Survival (PFS) is defined as the time from the date of randomization to the earliest evidence of documented Progressive Disease (PD) or of death from any cause. The date of global deterioration or symptomatic deterioration will not be used as the date of PD.

End point type	Secondary

End point timeframe:

Through study completion, an expected average of 1 year

End point values	NKTR-102	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	92	86		
Units: Months				
median (confidence interval 95%)	2.8 (2.0 to 4.1)	1.9 (1.9 to 2.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival in Brain Metastasis (PFS-BM)

End point title	Progression-Free Survival in Brain Metastasis (PFS-BM)

End point description:

Progression-Free Survival in Brain Metastasis (PFS-BM) is defined as the time from the date of randomization to the earliest evidence of documented Progressive Disease (PD) per Response Assessment in Neuro-Oncology—Brain Metastases (RANO-BM) in brain metastases or death from any cause. The PD will also be determined by the investigator's assessments.

End point type	Secondary

End point timeframe:

Through study completion, an expected average of 1 year

End point values	NKTR-102	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	92	86		
Units: Months				
median (confidence interval 95%)	3.9 (2.6 to 4.3)	3.3 (1.9 to 3.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (Overall)

End point title	Progression-Free Survival (Overall)

End point description:

Progression-free survival (CNS and peripheral) is defined as the time from the date of randomization to the earliest evidence of documented PD in either the CNS or peripheral (using RANO-BM) or death from any cause. The PD will be determined by both the investigator's and the central imaging facility assessments. The same statistical methods that were used for PFS and PFS-BM will be used for PFS (Overall).

End point type	Secondary

End point timeframe:

Through study completion, an expected average of 1 year

End point values	NKTR-102	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	92	86		
Units: Months				
median (confidence interval 95%)	2.1 (1.9 to 3.7)	1.9 (1.8 to 2.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rates (ORR) at the NKTR-102 Treatment and the Treatment of Physician's Choice (TPC)

End point title	Objective Response Rates (ORR) at the NKTR-102 Treatment and the Treatment of Physician's Choice (TPC)

End point description:

Objective Response Rate (ORR) will be defined as the proportion of patients with a confirmed Complete Response (CR) or Partial Response (PR) (RECIST for lesions outside the Central Nervous System (CNS); RANO-BM for CNS lesions) based upon the best response as assessed by the central imaging facility. As a secondary analysis, ORR will be calculated based on the Investigator assessment of response.

End point type	Secondary

End point timeframe:

Through study completion, an expected average of 1 year

End point values	NKTR-102	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	83	73		
Units: Participants				
Objective Response Rate (CR+PR)	4	2		
Stable Disease	16	5		
Progressive Disease	38	32		
Not Evaluable	18	30		
Missing	7	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Benefit Rate (CBR)

End point title	Clinical Benefit Rate (CBR)

End point description:

Clinical Benefit Rate will be defined as the proportion of patients having a Complete Response (CR), Partial Response (PR), or Stable Disease (SD) for at least 4 months (≥ 120 days). The SD duration of 4 months is selected to reflect the shorter life expectancy of study population. CBR will be calculated based on both the central imaging facility assessment of response, progression and stability of disease, as well as the investigator's assessment of these parameters.

End point type	Secondary

End point timeframe:

For at least 4 months, with an expected average of 1 year

End point values	NKTR-102	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	92	86		
Units: Participants				
Complete Response	0	0		
Partial Response	6	6		
Stable Disease >= 120 days	17	5		
Clinical Benefit Rate	23	11		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR)

End point title	Duration of Response (DoR)

End point description:

Duration of response (DoR) outside the CNS will be defined as the time from first documented CR or PR until the earliest evidence of disease progression per RECIST v1.1 or death from any cause. DoR will be calculated based on the central imaging facility assessment of response and progression as well as the investigator's assessment of response and progression.

End point type	Secondary

End point timeframe:

Through study completion, an expected average of 1 year

End point values	NKTR-102	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	83	73		
Units: Months				
median (inter-quartile range (Q1-Q3))	7.4 (7.3 to 16.4)	3.5 (3.5 to 3.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Compare Health-Related Quality of Life (HRQoL) Using the European Organisation for Treatment of Cancer (EORTC) Quality of Life Core 30 (QLQ-C30) Module With the Brain Neoplasms 20-question (BN-20) Subscale.

End point title	Compare Health-Related Quality of Life (HRQoL) Using the European Organisation for Treatment of Cancer (EORTC) Quality of Life Core 30 (QLQ-C30) Module With the Brain Neoplasms 20-question (BN-20) Subscale.

End point description:

The EORTC QLQ-BN20 Scale has a series of 20 questions each of which involve reporting a scale from 1-4. It is an increasing scale where a score of one indicates "not at all" while a score of four indicates "very much". The minimum score is 20 and the maximum score is 80. The higher the score the worse the outcome.

End point type	Secondary

End point timeframe:

Through study completion, an expected average of 1 year

End point values	NKTR-102	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	35		
Units: Change in QLQ-C30 Score				
arithmetic mean (standard error)	-12.29 (± 20.928)	-8.06 (± 21.888)		

Statistical analyses

No statistical analyses for this end point

Secondary: Compare Health-Related Quality of Life (HRQoL) Using the the EuroQoL 5D (EQ-5D-5L™)

End point title	Compare Health-Related Quality of Life (HRQoL) Using the the EuroQoL 5D (EQ-5D-5L™)

End point description:

The EQ-5D-5L scale is used to measure health by having a patient answer a series of questions. There are a series of 5 questions each of which is scaled from a score of 4-20 in increasing increments of 4. The scale is numbered from 0 to 100 where 100 means the beast health you can imagine and 0 means the worst health.

End point type	Secondary

End point timeframe:

Through study completion, an expected average of 1 year

End point values	NKTR-102	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	92	86		
Units: Change in EuroQol 5D Score				
arithmetic mean (standard error)	-6.00 (± 20.482)	-4.90 (± 20.112)		

Statistical analyses

No statistical analyses for this end point

Secondary: Compare Health-Related Quality of Life (HRQoL) Using the Brief Fatigue Inventory (BFI)

End point title	Compare Health-Related Quality of Life (HRQoL) Using the Brief Fatigue Inventory (BFI)

End point description:

The Brief Fatigue Inventory scale utilizes a series of 4 questions. The first three are scored with a scale from 1-10. The fourth question has 6 six sub components each of which are scored with a scale of 1-10. For every scale, a score of 0 indicates no fatigue/interference where a score of 10 indicates as bad as you can imagine. A patient's score can range from 0 to 100 where 0 indicates the best outcome and 100 indicates the worst.

End point type	Secondary

End point timeframe:

Through study completion, an expected average of 1 year

End point values	NKTR-102	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	92	86		
Units: Change in BFI Score				
arithmetic mean (standard deviation)	0.89 (± 1.924)	1.15 (± 2.004)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Adverse Events as Assessed by Common Terminology Criteria for Adverse Events (CTCAE) v4.3

End point title	Number of Participants With Adverse Events as Assessed by Common Terminology Criteria for Adverse Events (CTCAE) v4.3

End point description:

The number of participants with adverse events as assessed by Common Terminology Criteria for Adverse Events (CTCAE) v4.3

End point type	Secondary

End point timeframe:

Through study completion, an expected average of 1 year

End point values	NKTR-102	Treatment of Physician's Choice (TPC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90	77		
Units: Particpants	90	76		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The adverse event data was collected over the entire course of the study or approximately 2 years and 8 months.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	NKTR-102
Reporting group description: -	
Reporting group title	TREATMENT OF PHYSICIAN'S CHOICE

Reporting group description: -

Serious adverse events	NKTR-102	TREATMENT OF PHYSICIAN'S CHOICE	
Total subjects affected by serious adverse events			
subjects affected / exposed	33 / 90 (36.67%)	24 / 77 (31.17%)	
number of deaths (all causes)	60	57	
number of deaths resulting from adverse events			
Vascular disorders			
Deep Vein Thrombosis Grade 4			
subjects affected / exposed	0 / 90 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Generalized Physical Health Deterioration Grade 3			
subjects affected / exposed	1 / 90 (1.11%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalized Physical Health Deterioration Grade 5			
subjects affected / exposed	1 / 90 (1.11%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Asthenia Grade 3			

subjects affected / exposed	1 / 90 (1.11%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	2 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise Grade 3			
subjects affected / exposed	1 / 90 (1.11%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue Grade 2			
subjects affected / exposed	0 / 90 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	9 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue Grade 3			
subjects affected / exposed	0 / 90 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnea Grade 2			
subjects affected / exposed	0 / 90 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnea Grade 3			
subjects affected / exposed	0 / 90 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural Effusion Grade 3			
subjects affected / exposed	1 / 90 (1.11%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax Grade 2			
subjects affected / exposed	1 / 90 (1.11%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			

Confusional State Grade 2			
subjects affected / exposed	1 / 90 (1.11%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional State Grade 3			
subjects affected / exposed	0 / 90 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental Status Changes Grade 3			
subjects affected / exposed	1 / 90 (1.11%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hallucination Grade 4			
subjects affected / exposed	0 / 90 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Neutrophil count decreased			
subjects affected / exposed	0 / 90 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Hip Fracture Grade 3			
subjects affected / exposed	1 / 90 (1.11%)	2 / 77 (2.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion Grade 3			
subjects affected / exposed	0 / 90 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall Grade 3			
subjects affected / exposed	0 / 90 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac disorders			
Atrial Fibrillation Grade 3			
subjects affected / exposed	1 / 90 (1.11%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac Tamponade Grade 4			
subjects affected / exposed	0 / 90 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Fine motor skill dysfunction Grade 2			
subjects affected / exposed	1 / 90 (1.11%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain Edema Grade 3			
subjects affected / exposed	1 / 90 (1.11%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness Grade 3			
subjects affected / exposed	1 / 90 (1.11%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy Grade 2			
subjects affected / exposed	1 / 90 (1.11%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoesthesia Grade 2			
subjects affected / exposed	1 / 90 (1.11%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraesthesia Grade 2			
subjects affected / exposed	1 / 90 (1.11%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Seizure Grade 2			
subjects affected / exposed	1 / 90 (1.11%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope Grade 3			
subjects affected / exposed	1 / 90 (1.11%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status Epilepticus Grade 3			
subjects affected / exposed	0 / 90 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Neutropenia Grade 4			
subjects affected / exposed	3 / 90 (3.33%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	10 / 10	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia Grade 4			
subjects affected / exposed	1 / 90 (1.11%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile Neutropenia Grade 3			
subjects affected / exposed	0 / 90 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Normochromic Normocystic Anemia Grade 4			
subjects affected / exposed	0 / 90 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Blindness Grade 3			
subjects affected / exposed	0 / 90 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal disorders			
Diarrhea Grade 3			
subjects affected / exposed	5 / 90 (5.56%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	5 / 12	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal Obstruction Grade 3			
subjects affected / exposed	1 / 90 (1.11%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea Grade 2			
subjects affected / exposed	0 / 90 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	26 / 30	11 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis Grade 2			
subjects affected / exposed	1 / 90 (1.11%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis Grade 3			
subjects affected / exposed	3 / 90 (3.33%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	4 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting Grade 2			
subjects affected / exposed	3 / 90 (3.33%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	4 / 19	2 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting Grade 3			
subjects affected / exposed	0 / 90 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic Colitis Grade 4			
subjects affected / exposed	1 / 90 (1.11%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Esophagitis Grade 3			

subjects affected / exposed	1 / 90 (1.11%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal Pain Grade 2			
subjects affected / exposed	0 / 90 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	3 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal Pain Grade 3			
subjects affected / exposed	0 / 90 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia Grade 3			
subjects affected / exposed	0 / 90 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile Duct Stone Grade 3			
subjects affected / exposed	1 / 90 (1.11%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis Grade 3			
subjects affected / exposed	1 / 90 (1.11%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic Function Abnormal Grade 3			
subjects affected / exposed	1 / 90 (1.11%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperbilirubinemia Grade 3			
subjects affected / exposed	0 / 90 (0.00%)	2 / 77 (2.60%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic Failure Grade 3			

subjects affected / exposed	0 / 90 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Groin Pain Grade 2			
subjects affected / exposed	1 / 90 (1.11%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pathological Fracture Grade 3			
subjects affected / exposed	1 / 90 (1.11%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle Spasm Grade 3			
subjects affected / exposed	1 / 90 (1.11%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacteremia Grade 4			
subjects affected / exposed	0 / 90 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia Sepsis Grade 4			
subjects affected / exposed	0 / 90 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Esophageal Candidiasis Grade 3			
subjects affected / exposed	0 / 90 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyoderma Grade 3			
subjects affected / exposed	0 / 90 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Device Related Infection Grade 4			
subjects affected / exposed	1 / 90 (1.11%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device Related Sepsis Grade 4			
subjects affected / exposed	1 / 90 (1.11%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza Grade 4			
subjects affected / exposed	1 / 90 (1.11%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis Grade 3			
subjects affected / exposed	1 / 90 (1.11%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia Grade 3			
subjects affected / exposed	1 / 90 (1.11%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia Grade 5			
subjects affected / exposed	1 / 90 (1.11%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lung Infection Grade 3			
subjects affected / exposed	1 / 90 (1.11%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic Sepsis Grade 3			
subjects affected / exposed	1 / 90 (1.11%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary Tract Infection Grade 3			

subjects affected / exposed	1 / 90 (1.11%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	2 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral Gastroenteritis			
subjects affected / exposed	1 / 90 (1.11%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Failure to Thrive Grade 3			
subjects affected / exposed	0 / 90 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration Grade 3			
subjects affected / exposed	2 / 90 (2.22%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcemia Grade 3			
subjects affected / exposed	0 / 90 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatremia Grade 3			
subjects affected / exposed	1 / 90 (1.11%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased Appetite Grade 2			
subjects affected / exposed	0 / 90 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	2 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased Appetite Grade 3			
subjects affected / exposed	0 / 90 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back Pain Grade 3			

subjects affected / exposed	0 / 90 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	NKTR-102	TREATMENT OF PHYSICIAN'S CHOICE	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	90 / 90 (100.00%)	76 / 77 (98.70%)	
Investigations			
Neutrophil Count Decreased			
subjects affected / exposed	6 / 90 (6.67%)	10 / 77 (12.99%)	
occurrences (all)	9	14	
Aspartate Aminotransferase Increased			
subjects affected / exposed	5 / 90 (5.56%)	9 / 77 (11.69%)	
occurrences (all)	6	13	
Weight Decreased			
subjects affected / exposed	13 / 90 (14.44%)	1 / 77 (1.30%)	
occurrences (all)	15	1	
Alanine Aminotransferase Increased			
subjects affected / exposed	2 / 90 (2.22%)	9 / 77 (11.69%)	
occurrences (all)	3	13	
Platelet Count Decreased			
subjects affected / exposed	3 / 90 (3.33%)	4 / 77 (5.19%)	
occurrences (all)	5	10	
White blood cell count decreased			
subjects affected / exposed	2 / 90 (2.22%)	4 / 77 (5.19%)	
occurrences (all)	3	4	
Nervous system disorders			
Headache			
subjects affected / exposed	18 / 90 (20.00%)	9 / 77 (11.69%)	
occurrences (all)	26	11	
Dizziness			

subjects affected / exposed	9 / 90 (10.00%)	4 / 77 (5.19%)	
occurrences (all)	15	8	
Neuropathy Peripheral			
subjects affected / exposed	3 / 90 (3.33%)	9 / 77 (11.69%)	
occurrences (all)	3	13	
Dysgeusia			
subjects affected / exposed	7 / 90 (7.78%)	2 / 77 (2.60%)	
occurrences (all)	10	5	
Seizure			
subjects affected / exposed	2 / 90 (2.22%)	4 / 77 (5.19%)	
occurrences (all)	8	17	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	36 / 90 (40.00%)	26 / 77 (33.77%)	
occurrences (all)	43	31	
Asthenia			
subjects affected / exposed	28 / 90 (31.11%)	16 / 77 (20.78%)	
occurrences (all)	29	27	
Pyrexia			
subjects affected / exposed	6 / 90 (6.67%)	7 / 77 (9.09%)	
occurrences (all)	9	9	
Oedema Peripheral			
subjects affected / exposed	6 / 90 (6.67%)	5 / 77 (6.49%)	
occurrences (all)	12	8	
Pain			
subjects affected / exposed	5 / 90 (5.56%)	4 / 77 (5.19%)	
occurrences (all)	6	4	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	17 / 90 (18.89%)	18 / 77 (23.38%)	
occurrences (all)	35	28	
Anemia			
subjects affected / exposed	11 / 90 (12.22%)	17 / 77 (22.08%)	
occurrences (all)	14	21	
Thrombocytopenia			

subjects affected / exposed	5 / 90 (5.56%)	5 / 77 (6.49%)	
occurrences (all)	11	7	
Leukopenia			
subjects affected / exposed	5 / 90 (5.56%)	3 / 77 (3.90%)	
occurrences (all)	6	4	
Eye disorders			
Vision Blurred			
subjects affected / exposed	10 / 90 (11.11%)	2 / 77 (2.60%)	
occurrences (all)	10	3	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	54 / 90 (60.00%)	31 / 77 (40.26%)	
occurrences (all)	60	36	
Diarrhea			
subjects affected / exposed	66 / 90 (73.33%)	15 / 77 (19.48%)	
occurrences (all)	195	18	
Vomiting			
subjects affected / exposed	34 / 90 (37.78%)	17 / 77 (22.08%)	
occurrences (all)	65	24	
Constipation			
subjects affected / exposed	24 / 90 (26.67%)	20 / 77 (25.97%)	
occurrences (all)	40	21	
Abdominal Pain			
subjects affected / exposed	19 / 90 (21.11%)	11 / 77 (14.29%)	
occurrences (all)	30	17	
Upper Abdominal Pain			
subjects affected / exposed	6 / 90 (6.67%)	3 / 77 (3.90%)	
occurrences (all)	9	3	
Stomatitis			
subjects affected / exposed	4 / 90 (4.44%)	5 / 77 (6.49%)	
occurrences (all)	12	6	
Abdominal Distension			
subjects affected / exposed	7 / 90 (7.78%)	1 / 77 (1.30%)	
occurrences (all)	15	4	
Flatulence			

subjects affected / exposed	5 / 90 (5.56%)	1 / 77 (1.30%)	
occurrences (all)	7	4	
Dyspepsia			
subjects affected / exposed	5 / 90 (5.56%)	0 / 77 (0.00%)	
occurrences (all)	5	0	
Respiratory, thoracic and mediastinal disorders			
Dyspnea			
subjects affected / exposed	11 / 90 (12.22%)	14 / 77 (18.18%)	
occurrences (all)	21	19	
Cough			
subjects affected / exposed	9 / 90 (10.00%)	7 / 77 (9.09%)	
occurrences (all)	13	8	
Oropharyngeal Pain			
subjects affected / exposed	5 / 90 (5.56%)	1 / 77 (1.30%)	
occurrences (all)	6	1	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	10 / 90 (11.11%)	9 / 77 (11.69%)	
occurrences (all)	16	9	
Pruritus			
subjects affected / exposed	6 / 90 (6.67%)	4 / 77 (5.19%)	
occurrences (all)	8	4	
Rash			
subjects affected / exposed	3 / 90 (3.33%)	5 / 77 (6.49%)	
occurrences (all)	5	7	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	8 / 90 (8.89%)	5 / 77 (6.49%)	
occurrences (all)	9	5	
Anxiety			
subjects affected / exposed	2 / 90 (2.22%)	6 / 77 (7.79%)	
occurrences (all)	8	8	
Depression			
subjects affected / exposed	6 / 90 (6.67%)	2 / 77 (2.60%)	
occurrences (all)	7	3	
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	5 / 90 (5.56%)	9 / 77 (11.69%)	
occurrences (all)	5	12	
Pain in Extremity			
subjects affected / exposed	6 / 90 (6.67%)	8 / 77 (10.39%)	
occurrences (all)	7	10	
Back pain			
subjects affected / exposed	5 / 90 (5.56%)	7 / 77 (9.09%)	
occurrences (all)	6	9	
Muscle Spasms			
subjects affected / exposed	8 / 90 (8.89%)	2 / 77 (2.60%)	
occurrences (all)	8	3	
Myalgia			
subjects affected / exposed	2 / 90 (2.22%)	8 / 77 (10.39%)	
occurrences (all)	3	10	
Muscle Weakness			
subjects affected / exposed	5 / 90 (5.56%)	3 / 77 (3.90%)	
occurrences (all)	6	4	
Bone Pain			
subjects affected / exposed	5 / 90 (5.56%)	1 / 77 (1.30%)	
occurrences (all)	5	2	
Musculoskeletal Pain			
subjects affected / exposed	0 / 90 (0.00%)	4 / 77 (5.19%)	
occurrences (all)	0	8	
Infections and infestations			
Urinary Tract Infection			
subjects affected / exposed	8 / 90 (8.89%)	3 / 77 (3.90%)	
occurrences (all)	6	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	33 / 90 (36.67%)	14 / 77 (18.18%)	
occurrences (all)	41	21	
Hypokalemia			
subjects affected / exposed	16 / 90 (17.78%)	4 / 77 (5.19%)	
occurrences (all)	34	13	
Dehydration			

subjects affected / exposed	9 / 90 (10.00%)	1 / 77 (1.30%)	
occurrences (all)	13	3	
Hypocalcemia			
subjects affected / exposed	8 / 90 (8.89%)	1 / 77 (1.30%)	
occurrences (all)	18	2	
Hypoalbuminemia			
subjects affected / exposed	5 / 90 (5.56%)	1 / 77 (1.30%)	
occurrences (all)	14	2	

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