Clinical trial results:
A randomized phase II trial of metronomic oral vinorelbine plus cyclophosphamide and capecitabine (VEX) versus weekly paclitaxel as first or second-line treatment in patients with ER-positive/HER2-negative advanced or metastatic breast cancer

Summary

EudraCT number	2016-002200-39
Trial protocol	IT
Global end of trial date	23 November 2022
Results information	
Result version number	v1 (current)
This version publication date	29 March 2024
First version publication date	29 March 2024

Trial information

Trial identification	
Sponsor protocol code	IBCSG 54-16
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02954055
WHO universal trial number (UTN)	-

Notes:

Sponsors	
Sponsor organisation name	ETOP IBCSG Partners Foundation
Sponsor organisation address	Effingerstrasse 33, Bern, Switzerland, 3008
Public contact	ETOP IBCSG Partners Foundation, ETOP IBCSG Partners Foundation, +41 31 511 94 00, ibcsg-regulatory@etop.ibcsg.org
Scientific contact	ETOP IBCSG Partners Foundation, ETOP IBCSG Partners Foundation, +41 31 511 94 00, ibcsg-regulatory@etop.ibcsg.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	04 December 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 November 2021
Global end of trial reached?	Yes
Global end of trial date	23 November 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess efficacy, as measured by the time to treatment failure (TTF), of the first-line combination treatment with vinorelbine, cyclophosphamide and capecitabine (VEX) in comparison with paclitaxel monotherapy in ER+/HER2–, metastatic or locally advanced breast cancer patients, who have progressed under previous endocrine therapy.

Protection of trial subjects:

Participating institutions' ethics committees or Institutional Review Boards approved the trial according to local laws and regulations. All patients gave written informed consent, and the trial was performed in compliance with the Helsinki Declaration. The Data Safety and Monitoring Board reviewed the data from this research throughout the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 September 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	Italy: 140
Worldwide total number of subjects	140
EEA total number of subjects	140

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)	91
From 65 to 84 years	49

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

METEORA was activated on 13 February 2017. METEORA enrolled 140 patients in 15 centers in Italy between 13 September 2017 and 14 January 2021

Pre-assignment

Screening details:

Written Informed Consent (IC) was signed and dated by the patient and the Investigator prior to starting screening procedures and randomization.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Paclitaxel

Arm description:

Paclitaxel 90 mg/m2 days 1, 8, 15 q4weeks. Patients will continue to receive assigned treatment until progression or lack of tolerability.

Arm type	Active comparator
Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Paclitaxel 90 mg/m2 i.v. days 1, 8, 15 every 4 weeks, according to standard local practice

Arm title	Metronomic VEX

Arm description:

Cyclophosphamide 50 mg orally once daily continuously, capecitabine 500 mg, orally 3 times a day (1500 mg/day) continuously, vinorelbine 40 mg orally days 1, 3, 5 each week continuously. Patients will continue to receive assigned treatment until progression or lack of tolerability.

Cyclophosphamide: Arm B

Capecitabine: Arm B

Vinorelbine: Arm B

Arm type	Experimental
Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	Endoxan Baxter
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Cyclophosphamide 50 mg orally once daily around 9am

Investigational medicinal product name	Capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet

Routes of administration	Oral use

Dosage and administration details:

Capecitabine 500 mg, orally 3 times a day (total 1500 mg/day) within 30 minutes after meals (breakfast, lunch, dinner)

Investigational medicinal product name	Vinorelbine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Vinorelbine 40 mg orally days 1, 3, 5 each week (Monday, Wednesday, Friday) after lunch

Number of subjects in period 1	Paclitaxel	Metronomic VEX
Started	69	71
Completed	63	70
Not completed	6	1
Did not initiate therapy	6	1

Baseline characteristics

Reporting groups

Reporting group title	Paclitaxel

Reporting group description:

Paclitaxel 90 mg/m2 days 1, 8, 15 q4weeks. Patients will continue to receive assigned treatment until progression or lack of tolerability.

Reporting group title	Metronomic VEX

Reporting group description:

Cyclophosphamide 50 mg orally once daily continuously, capecitabine 500 mg, orally 3 times a day (1500 mg/day) continuously, vinorelbine 40 mg orally days 1, 3, 5 each week continuously. Patients will continue to receive assigned treatment until progression or lack of tolerability.

Cyclophosphamide: Arm B

Capecitabine: Arm B

Vinorelbine: Arm B

Reporting group values	Paclitaxel	Metronomic VEX	Total
Number of subjects	69	71	140
Age categorical Units: Subjects			
Adults (18-64 years)	43	48	91
From 65-84 years	26	23	49
Gender categorical Units: Subjects			
Female	69	71	140
Male	0	0	0

Subject analysis sets

Subject analysis set title	Analysis Population Paclitaxel
Subject analysis set type	Intention-to-treat

Subject analysis set description:

• Efficacy analysis population: All randomized patients who receive at least one dose of trial treatment.
• Safety population: All randomized patients who receive at least one dose of trial treatment will be included in assessments of safety and tolerability.
(thus the two populations are the same)

Subject analysis set title	Analysis Population VEX
Subject analysis set type	Intention-to-treat

Subject analysis set description:

• Efficacy analysis population: All randomized patients who receive at least one dose of trial treatment.
• Safety population: All randomized patients who receive at least one dose of trial treatment will be included in assessments of safety and tolerability.
(thus the two populations are the same)

Reporting group values	Analysis Population Paclitaxel	Analysis Population VEX	
Number of subjects	63	70	
Age categorical Units: Subjects			
Adults (18-64 years)	41	47	

From 65-84 years	22	23	

Gender categorical Units: Subjects			
Female	63	70	
Male	0	0	

End points

End points reporting groups

Reporting group title	Paclitaxel

Reporting group description:

Paclitaxel 90 mg/m2 days 1, 8, 15 q4weeks. Patients will continue to receive assigned treatment until progression or lack of tolerability.

Reporting group title	Metronomic VEX

Reporting group description:

Cyclophosphamide 50 mg orally once daily continuously, capecitabine 500 mg, orally 3 times a day (1500 mg/day) continuously, vinorelbine 40 mg orally days 1, 3, 5 each week continuously. Patients will continue to receive assigned treatment until progression or lack of tolerability.

Cyclophosphamide: Arm B

Capecitabine: Arm B

Vinorelbine: Arm B

Subject analysis set title	Analysis Population Paclitaxel
Subject analysis set type	Intention-to-treat

Subject analysis set description:

• Efficacy analysis population: All randomized patients who receive at least one dose of trial treatment.
• Safety population: All randomized patients who receive at least one dose of trial treatment will be included in assessments of safety and tolerability.
(thus the two populations are the same)

Subject analysis set title	Analysis Population VEX
Subject analysis set type	Intention-to-treat

Subject analysis set description:

• Efficacy analysis population: All randomized patients who receive at least one dose of trial treatment.
• Safety population: All randomized patients who receive at least one dose of trial treatment will be included in assessments of safety and tolerability.
(thus the two populations are the same)

Primary: Time to Treatment Failure (TTF)

End point title	Time to Treatment Failure (TTF)

End point description:

Efficacy and tolerability, measured by time to treatment failure, of metronomic oral vinorelbine plus cyclophosphamide and capecitabine (VEX) versus weekly paclitaxel, using an intent-to-treat analysis approach.

End point type	Primary

End point timeframe:

Assessed at the start of every 4-week (28-day) treatment cycle from randomization to the end of treatment date or discontinuation; median follow-up was 29 months, with a minimum of 0.2 months and maximum of 48.5 months.

End point values	Analysis Population Paclitaxel	Analysis Population VEX		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	63	70		
Units: month				
median (standard error)	5.7 (± 0.06)	8.3 (± 0.06)		

Statistical analyses

Statistical analysis title	Statistical analysis primary endpoint
Comparison groups	Analysis Population Paclitaxel v Analysis Population VEX
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.008
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.42
upper limit	0.88

Secondary: Disease Control

End point title	Disease Control

End point description:

Defined as best overall response of complete response (CR) or partial response (PR), or stable disease (SD) (or non-CR/non-PD in the case of non-measurable disease only) lasting for at least 24 weeks (at least 2 scans), measured from randomization until first documentation of progressive disease. Best overall response was defined as best response recorded from randomization across all time points until disease progression. Confirmation of partial or complete response by an additional scan was not requested in this trial. Disease response and progression were assessed according to the revised Response Evaluation Criteria in Solid Tumors (RECIST version 1.1)

End point type	Secondary

End point timeframe:

Tumor measurements were assessed at baseline, and every 12 weeks (± 2 weeks) from randomization until first disease progression on the basis of clinical and radiological tumor assessments, on average approximately 9 months.

End point values	Analysis Population Paclitaxel	Analysis Population VEX		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	63	70		
Units: Participants				
Complete response (CR)	1	1		
Partial response (PR)	18	22		
Stable disease (SD)/ non-CR/non-PD	25	32		
Progressive disease	18	11		

Not evaluable	1	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)

End point description:

PFS was defined as time from randomization until documented disease progression according to Response Evaluation Criteria in Solid Tumors (RECIST 1.1) criteria or death, whichever occurred first; the death must have occurred within an interval of time corresponding to the interval of tumor re-evaluations. For patients without progression, follow-up was censored at the date of last disease assessment.

End point type	Secondary

End point timeframe:

Tumor measurements were assessed at baseline, and every 12 weeks (± 2 weeks) from randomization until first disease progression on the basis of clinical and radiological tumor assessments, on average approximately 9 months.

End point values	Analysis Population Paclitaxel	Analysis Population VEX		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	63	70		
Units: month				
median (standard error)	6.9 (± 0.06)	11.1 (± 0.05)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

Overall survival from time of randomisation will be summarised for each treatment group.

End point type	Secondary

End point timeframe:

From day 1 of cycle 1 until death from any cause (censored at date of last assessment of vital status for patients lost to follow up), assessed up to 36 months from the enrollment of the first patient.

End point values	Analysis Population Paclitaxel	Analysis Population VEX		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	63	70		
Units: month				
median (standard error)	33.7 (± 0.03)	29.5 (± 0.03)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events (AEs) were collected from the first dose of trial medication, at day 1 of every treatment cycle, until 28 days after all treatment discontinuation (end of treatment visit), regardless of whether it is considered related to a medication.

Adverse event reporting additional description:

AEs were collected from the first dose of trial medication until 28 days after all treatment discontinuation (EOT visit), regardless of whether it is considered related to a medication. The main criterion for tolerability is the occurrence of toxicities and adverse events.

Assessment type	Systematic

Dictionary used

Dictionary name	NCI CTCAE
Dictionary version	4.0

Reporting groups

Reporting group title	Analysis Population Paclitaxel
Reporting group description: -	
Reporting group title	Analysis Population VEX

Reporting group description: -

Serious adverse events	Analysis Population Paclitaxel	Analysis Population VEX	
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 63 (28.57%)	31 / 70 (44.29%)	
number of deaths (all causes)	1	3	
number of deaths resulting from adverse events			
Investigations			
Neutrophil count decreased			
subjects affected / exposed	8 / 63 (12.70%)	20 / 70 (28.57%)	
occurrences causally related to treatment / all	13 / 13	28 / 28	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 63 (0.00%)	3 / 70 (4.29%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alanine aminotransferase increased			
subjects affected / exposed	0 / 63 (0.00%)	2 / 70 (2.86%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alkaline phosphatase increased			

subjects affected / exposed	1 / 63 (1.59%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphocyte count decreased			
subjects affected / exposed	0 / 63 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
White blood cell decreased			
subjects affected / exposed	1 / 63 (1.59%)	12 / 70 (17.14%)	
occurrences causally related to treatment / all	0 / 1	12 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Pulmonary valve disease			
subjects affected / exposed	0 / 63 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	0 / 63 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Peripheral sensory neuropathy			
subjects affected / exposed	6 / 63 (9.52%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	8 / 8	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 63 (3.17%)	5 / 70 (7.14%)	
occurrences causally related to treatment / all	2 / 2	6 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Fatigue			

subjects affected / exposed	0 / 63 (0.00%)	4 / 70 (5.71%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Allergic reaction			
subjects affected / exposed	1 / 63 (1.59%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylaxis			
subjects affected / exposed	1 / 63 (1.59%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 63 (1.59%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 63 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 63 (0.00%)	2 / 70 (2.86%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 63 (0.00%)	2 / 70 (2.86%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	1 / 63 (1.59%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Nail discolouration			
subjects affected / exposed	0 / 63 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Palmar-plantar erythrodysesthesia syndrome			
subjects affected / exposed	0 / 63 (0.00%)	4 / 70 (5.71%)	
occurrences causally related to treatment / all	0 / 0	10 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Infections			
subjects affected / exposed	0 / 63 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	0 / 63 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatremia			
subjects affected / exposed	0 / 63 (0.00%)	2 / 70 (2.86%)	
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: 0 %

Non-serious adverse events	Analysis Population Paclitaxel	Analysis Population VEX	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	63 / 63 (100.00%)	70 / 70 (100.00%)	
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 63 (1.59%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	36 / 63 (57.14%)	31 / 70 (44.29%)	
occurrences (all)	131	151	
Injection site reaction			
subjects affected / exposed	2 / 63 (3.17%)	0 / 70 (0.00%)	
occurrences (all)	2	0	
Sudden death NOS			
subjects affected / exposed	0 / 63 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Immune system disorders			
Allergic reaction			
subjects affected / exposed	6 / 63 (9.52%)	2 / 70 (2.86%)	
occurrences (all)	8	2	
Anaphylaxis			
subjects affected / exposed	1 / 63 (1.59%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	0 / 63 (0.00%)	2 / 70 (2.86%)	
occurrences (all)	0	2	
Pulmonary edema			
subjects affected / exposed	0 / 63 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders - Other			
subjects affected / exposed	0 / 63 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Investigations			
Neutrophil count decreased			
subjects affected / exposed	13 / 63 (20.63%)	11 / 70 (15.71%)	
occurrences (all)	62	49	
Asparate aminotransferase increased			
subjects affected / exposed	19 / 63 (30.16%)	14 / 70 (20.00%)	
occurrences (all)	35	49	
Alkaline phosphatase increased			
subjects affected / exposed	1 / 63 (1.59%)	0 / 70 (0.00%)	
occurrences (all)	1	0	

Blood bilirubin increased			
subjects affected / exposed	0 / 63 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
GGT increased			
subjects affected / exposed	1 / 63 (1.59%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Fracture			
subjects affected / exposed	0 / 63 (0.00%)	2 / 70 (2.86%)	
occurrences (all)	0	2	
Hip fracture			
subjects affected / exposed	1 / 63 (1.59%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 63 (1.59%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Aortic valve disease			
subjects affected / exposed	0 / 63 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Artial flutter			
subjects affected / exposed	0 / 63 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Supraventricular tachycardia			
subjects affected / exposed	3 / 63 (4.76%)	4 / 70 (5.71%)	
occurrences (all)	3	6	
Ventricular arrhythmia			
subjects affected / exposed	1 / 63 (1.59%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Depressed level of consciousness			
subjects affected / exposed	0 / 63 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Facial nerve disorder			
subjects affected / exposed	0 / 63 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	

Optic nerve disorder			
subjects affected / exposed	1 / 63 (1.59%)	2 / 70 (2.86%)	
occurrences (all)	1	2	
Peripheral sensory neuropathy			
subjects affected / exposed	30 / 63 (47.62%)	5 / 70 (7.14%)	
occurrences (all)	228	40	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	41 / 63 (65.08%)	26 / 70 (37.14%)	
occurrences (all)	233	154	
Thrombocytopenia			
subjects affected / exposed	2 / 63 (3.17%)	10 / 70 (14.29%)	
occurrences (all)	3	38	
Eye disorders			
Cataract			
subjects affected / exposed	0 / 63 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	1 / 63 (1.59%)	2 / 70 (2.86%)	
occurrences (all)	1	3	
Constipation			
subjects affected / exposed	13 / 63 (20.63%)	6 / 70 (8.57%)	
occurrences (all)	25	13	
Diarrhoea			
subjects affected / exposed	12 / 63 (19.05%)	22 / 70 (31.43%)	
occurrences (all)	23	63	
Mucositis oral			
subjects affected / exposed	7 / 63 (11.11%)	5 / 70 (7.14%)	
occurrences (all)	14	13	
Nausea			
subjects affected / exposed	17 / 63 (26.98%)	30 / 70 (42.86%)	
occurrences (all)	34	154	
Vomiting			
subjects affected / exposed	9 / 63 (14.29%)	8 / 70 (11.43%)	
occurrences (all)	9	35	
Skin and subcutaneous tissue disorders			

Alopecia			
subjects affected / exposed	21 / 63 (33.33%)	2 / 70 (2.86%)	
occurrences (all)	138	9	
Palmar-plantar erythrodysesthesia syndrome			
subjects affected / exposed	5 / 63 (7.94%)	5 / 70 (7.14%)	
occurrences (all)	23	38	
Musculoskeletal and connective tissue disorders			
Arthralgia and/or myalgia			
subjects affected / exposed	22 / 63 (34.92%)	20 / 70 (28.57%)	
occurrences (all)	75	84	
Infections and infestations			
Infection			
subjects affected / exposed	20 / 63 (31.75%)	14 / 70 (20.00%)	
occurrences (all)	48	42	
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	1 / 63 (1.59%)	5 / 70 (7.14%)	
occurrences (all)	1	19	
Hyperglycemia			
subjects affected / exposed	1 / 63 (1.59%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Hyponatremia			
subjects affected / exposed	1 / 63 (1.59%)	1 / 70 (1.43%)	
occurrences (all)	1	1	

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