Clinical trial results:
Circulating tumor DNA guiding (Olaparib) Lynparza® treatment in Ovarian Cancer (CLIO). Establishing the value of a ctDNA-based HRD assay for predicting olaparib response in women with relapsed ovarian cancer

Summary

EudraCT number	2015-005838-22
Trial protocol	BE
Global end of trial date	09 March 2021
Results information	
Result version number	v1 (current)
This version publication date	21 November 2024
First version publication date	21 November 2024
Summary attachment (see zip file)	2015-005838-22_Paper (CLIO_paper.pdf)

Trial information

Trial identification	
Sponsor protocol code	CLIO
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02822157
WHO universal trial number (UTN)	-

Notes:

Sponsors	
Sponsor organisation name	BGOG
Sponsor organisation address	Herestraat 49, Leuven, Belgium, 3000
Public contact	Joke De Roover, UZLeuven, 32 16347419, joke.deroover@uzleuven.be
Scientific contact	Joke De Roover, UZLeuven, 32 16347419, joke.deroover@uzleuven.be

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	16 April 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 March 2021
Global end of trial reached?	Yes
Global end of trial date	09 March 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Demonstrate the value of a ctDNA-based assay for homologous recombination deficiency to predict response to olaparib monotherapy. This analysis will also be performed according to platinum-sensitivity (platinum-sensitive versus platinum-resistant).

Protection of trial subjects:

Trial visits and assessments were balanced to ensure patients are sufficiently closely monitored. The number and type of visits and assessments requested were required to follow-up on patient safety.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2016
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	Belgium: 160
Worldwide total number of subjects	160
EEA total number of subjects	160

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)	78
From 65 to 84 years	81
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Recruitment was solely performed in UZLeuven (Belgium). FPI was on 20Sep2016, LPI was on 04Feb2019.

Pre-assignment

Screening details:

Platinum sensitive or resistant ovarian cancer patients with measurable disease and >1 prior line of chemotherapy randomized (2:1) to Olaparib or physician's choice chemotherapy (CT). CTwas administered according to local guidelines, Olaparib continued until disease progression, toxicity or WOC. Cross-over from CT to Olaparib was possible after PD.

Period 1

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

Blinding implementation details:

NAP, study was not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Olaparib

Arm description:

Olaparib

Arm type	Experimental
Investigational medicinal product name	Olaparib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

300 mg BID

Arm title	Physician's choice chemotherapy

Arm description:

Physician's choice chemotherapy

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

Dosage and administration details:

AUC4 on day 1 of a 3-weekly schedule when combined with Gemcitabin
AUC5 on day 1 of a 3-weekly schedule when combined with Paclitaxel
AUC5 on day 1 of a 4-weekly schedule when combined with Caelyx

Investigational medicinal product name	Gemcitabin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion

Routes of administration	Intravenous use
Dosage and administration details: 1000mg/m² on day 1 and day 8 of a three-weekly schedule when combined with Carboplatin 1000mg/m² on day 1, day 8 and day 15 of a four-weekly schedule when given alone	
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: 175mg/m² on day 1 of a three-weekly schedule when combined with Carboplatin 80mg/m² on day 1, day 8 and day 15 of a four-weekly schedule when given alone	
Investigational medicinal product name	Caelyx
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 30mg/m² on day 1 of a 4-weekly schedule when given in combination with Carboplatin 40mg/m² on day 1 of a 4-weekly schedule when given alone	
Investigational medicinal product name	Topotecan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 1.25mg/m² of day 1 to 5 of a three-weekly schedule	

Number of subjects in period 1	Olaparib	Physician's choice chemotherapy
Started	107	53
Completed	2	0
Not completed	105	53
Adverse event, serious fatal	2	-
Consent withdrawn by subject	2	-
Lost to follow-up	1	-
Lack of efficacy	100	53

Baseline characteristics

Reporting groups	
Reporting group title	Olaparib
Reporting group description: Olaparib	
Reporting group title	Physician's choice chemotherapy
Reporting group description: Physician's choice chemotherapy	

Reporting group values	Olaparib	Physician's choice chemotherapy	Total
Number of subjects	107	53	160
Age categorical			
Age			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Median age			0
Age continuous			
Age			
Units: years			
median	63	63	
inter-quartile range (Q1-Q3)	57 to 70	59 to 70	-
Gender categorical			
Gender			
Units: Subjects			
Female	107	53	160
Male	0	0	0
Race			
Race			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	0	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	106	53	159
More than one race	0	0	0
Unknown or Not Reported	0	0	0
WHO			

WHO			
Units: Subjects			
WHO score 0	59	30	89
WHO score 1	46	22	68
WHO score 2	2	1	3
Platinum sensitivity			
Platinum sensitivity			
Units: Subjects			
Platinum-resistant ovarian cancer	67	33	100
Platinum-sensitive ovarian cancer	40	20	60
Histology			
Histology			
Units: Subjects			
High-grade endometrioid ovarian cancer	1	0	1
High-grade serous ovarian cancer	98	49	147
Malignant mixed Müllerian tumor	1	0	1
Ovarian clear-cell carcinoma	7	4	11
BRCA status			
BRCA status			
Units: Subjects			
Germiline BRCA1	12	2	14
Germline BRCA2	3	0	3
Somatic BRCA1	2	2	4
Somatic BRCA2	1	0	1
None	89	49	138
Previous Bevacizumab			
Previous Bevacizumab			
Units: Subjects			
Yes	57	24	81
No	50	29	79
Previous PARP inhibitor			
Previous PARP inhibitor			
Units: Subjects			
Yes	5	3	8
No	97	46	143
Possible	5	4	9
Prior lines of systemic therapy			
Prior lines of systemic therapy			
Units: Subjects			
1 prior line of systemic therapy	19	10	29
2 prior lines of systemic therapy	24	17	41
3 prior lines of systemic therapy	24	8	32
4 prior lines of systemic therapy	20	11	31
5 prior lines of systemic therapy	10	2	12
6 prior lines of systemic therapy	3	2	5
8 prior lines of systemic therapy	5	2	7
7 prior lines of systemic therapy	2	1	3
Prior lines per category			
Prior lines per category			
Units: Subjects			

3 or less	67	35	102
4 or more	40	18	58

End points

End points reporting groups	
Reporting group title	Olaparib
Reporting group description: Olaparib	
Reporting group title	Physician's choice chemotherapy
Reporting group description: Physician's choice chemotherapy	

Primary: Overall Objective Response	
End point title	Overall Objective Response
End point description: Objective response rade, exclusing non-evaluable cases	
End point type	Primary
End point timeframe: 1 year after end inclusion	

End point values	Olaparib	Physician's choice chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107	53		
Units: %	26	15		

Statistical analyses

Statistical analysis title	Fisher's exact test
Comparison groups	Olaparib v Physician's choice chemotherapy
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.701
Method	Fisher exact

Secondary: Clinical Benefit Rate	
End point title	Clinical Benefit Rate
End point description: Clinical benefit rate, excluding non-evaluable cases	
End point type	Secondary

End point timeframe:

1 year after end inclusion

End point values	Olaparib	Physician's choice chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107	53		
Units: %	58	30		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 4 years, 6 months	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.1
Reporting groups	
Reporting group title	Olaparib
Reporting group description: Olaparib	
Reporting group title	Physician's choice chemotherapy
Reporting group description: Physician's choice chemotherapy	

Serious adverse events	Olaparib	Physician's choice chemotherapy	
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 107 (7.48%)	5 / 53 (9.43%)	
number of deaths (all causes)	3	4	
number of deaths resulting from adverse events	3	4	
Surgical and medical procedures			
Surgical procedure			
subjects affected / exposed	1 / 107 (0.93%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Abdominal pain			
subjects affected / exposed	2 / 107 (1.87%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 107 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Flank pain			

subjects affected / exposed	1 / 107 (0.93%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General deterioration			
subjects affected / exposed	7 / 107 (6.54%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	0 / 10	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 107 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General malaise			
subjects affected / exposed	1 / 107 (0.93%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 107 (0.93%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Allergic reaction			
subjects affected / exposed	0 / 107 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	5 / 107 (4.67%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Uterine hemorrhage			
subjects affected / exposed	1 / 107 (0.93%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory, thoracic and mediastinal disorders			
Dyspnea			
subjects affected / exposed	3 / 107 (2.80%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 107 (0.93%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 107 (1.87%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carbonarcosis			
subjects affected / exposed	1 / 107 (0.93%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusion			
subjects affected / exposed	1 / 107 (0.93%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Intracranial hemorrhage			
subjects affected / exposed	1 / 107 (0.93%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal canal stenosis			
subjects affected / exposed	0 / 107 (0.00%)	1 / 53 (1.89%)	
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			
Anemia			

subjects affected / exposed	5 / 107 (4.67%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	3 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ascites			
subjects affected / exposed	4 / 107 (3.74%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Capillary leak syndrome			
subjects affected / exposed	0 / 107 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hemolytic uremic syndrome			
subjects affected / exposed	0 / 107 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	1 / 107 (0.93%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelodysplastic syndrome			
subjects affected / exposed	1 / 107 (0.93%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 107 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colonic hemorrhage			
subjects affected / exposed	1 / 107 (0.93%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon obstruction			

subjects affected / exposed	1 / 107 (0.93%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon perforation			
subjects affected / exposed	1 / 107 (0.93%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 1	
Small bowel obstruction			
subjects affected / exposed	1 / 107 (0.93%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastro-intestinal pain			
subjects affected / exposed	1 / 107 (0.93%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 107 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	3 / 107 (2.80%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal perforation			
subjects affected / exposed	1 / 107 (0.93%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hepatobiliary disorders			
Liver hematoma			
subjects affected / exposed	1 / 107 (0.93%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			

subjects affected / exposed	2 / 107 (1.87%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary carcinomatosis			
subjects affected / exposed	0 / 107 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney insufficiency			
subjects affected / exposed	0 / 107 (0.00%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 107 (0.93%)	3 / 53 (5.66%)	
occurrences causally related to treatment / all	0 / 1	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 107 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture			
subjects affected / exposed	1 / 107 (0.93%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Device-related infection			
subjects affected / exposed	1 / 107 (0.93%)	2 / 53 (3.77%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Fever			
subjects affected / exposed	3 / 107 (2.80%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Flu-like symptoms			
subjects affected / exposed	1 / 107 (0.93%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection of unknown origin			
subjects affected / exposed	3 / 107 (2.80%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypocalcaemia			
subjects affected / exposed	0 / 107 (0.00%)	1 / 53 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatremia			
subjects affected / exposed	1 / 107 (0.93%)	0 / 53 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Olaparib	Physician's choice chemotherapy	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	46 / 107 (42.99%)	21 / 53 (39.62%)	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	23 / 107 (21.50%)	12 / 53 (22.64%)	
occurrences (all)	25	15	
Headache			
subjects affected / exposed	8 / 107 (7.48%)	4 / 53 (7.55%)	
occurrences (all)	11	5	
Abdominal bloating			
subjects affected / exposed	4 / 107 (3.74%)	6 / 53 (11.32%)	
occurrences (all)	5	7	
General malaise			

subjects affected / exposed	4 / 107 (3.74%)	4 / 53 (7.55%)	
occurrences (all)	4	6	
Abdominal pain			
subjects affected / exposed	10 / 107 (9.35%)	4 / 53 (7.55%)	
occurrences (all)	10	5	
Alopecia			
subjects affected / exposed	2 / 107 (1.87%)	5 / 53 (9.43%)	
occurrences (all)	2	5	
Ascites			
subjects affected / exposed	5 / 107 (4.67%)	3 / 53 (5.66%)	
occurrences (all)	7	3	
Asthenia			
subjects affected / exposed	3 / 107 (2.80%)	3 / 53 (5.66%)	
occurrences (all)	3	3	
Dizziness			
subjects affected / exposed	6 / 107 (5.61%)	3 / 53 (5.66%)	
occurrences (all)	6	3	
Insomnia			
subjects affected / exposed	6 / 107 (5.61%)	2 / 53 (3.77%)	
occurrences (all)	6	2	
Respiratory, thoracic and mediastinal disorders			
Dyspnea			
subjects affected / exposed	12 / 107 (11.21%)	6 / 53 (11.32%)	
occurrences (all)	13	10	
Cough			
subjects affected / exposed	6 / 107 (5.61%)	9 / 53 (16.98%)	
occurrences (all)	6	11	
Epistaxis			
subjects affected / exposed	1 / 107 (0.93%)	4 / 53 (7.55%)	
occurrences (all)	1	4	
Bronchitis			
subjects affected / exposed	7 / 107 (6.54%)	1 / 53 (1.89%)	
occurrences (all)	7	1	
Psychiatric disorders			

Depression			
subjects affected / exposed	1 / 107 (0.93%)	3 / 53 (5.66%)	
occurrences (all)	1	3	
Cardiac disorders			
Palpitations			
subjects affected / exposed	2 / 107 (1.87%)	3 / 53 (5.66%)	
occurrences (all)	3	3	
Nervous system disorders			
Peripheral neuropathy			
subjects affected / exposed	4 / 107 (3.74%)	3 / 53 (5.66%)	
occurrences (all)	4	5	
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	19 / 107 (17.76%)	11 / 53 (20.75%)	
occurrences (all)	57	43	
Neutropenia			
subjects affected / exposed	5 / 107 (4.67%)	5 / 53 (9.43%)	
occurrences (all)	5	11	
Edema legs			
subjects affected / exposed	6 / 107 (5.61%)	3 / 53 (5.66%)	
occurrences (all)	8	5	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 107 (0.93%)	3 / 53 (5.66%)	
occurrences (all)	1	3	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	27 / 107 (25.23%)	11 / 53 (20.75%)	
occurrences (all)	33	21	
Vomiting			
subjects affected / exposed	22 / 107 (20.56%)	9 / 53 (16.98%)	
occurrences (all)	31	14	
Diarrhoea			
subjects affected / exposed	10 / 107 (9.35%)	8 / 53 (15.09%)	
occurrences (all)	12	11	
Small bowel obstruction			

subjects affected / exposed	9 / 107 (8.41%)	3 / 53 (5.66%)	
occurrences (all)	12	5	
Constipation			
subjects affected / exposed	9 / 107 (8.41%)	11 / 53 (20.75%)	
occurrences (all)	10	11	
Abdominal cramping			
subjects affected / exposed	5 / 107 (4.67%)	6 / 53 (11.32%)	
occurrences (all)	6	6	
Stomach pain			
subjects affected / exposed	8 / 107 (7.48%)	6 / 53 (11.32%)	
occurrences (all)	9	6	
Pyrosis			
subjects affected / exposed	7 / 107 (6.54%)	2 / 53 (3.77%)	
occurrences (all)	7	2	
Skin and subcutaneous tissue disorders			
Itch			
subjects affected / exposed	0 / 107 (0.00%)	3 / 53 (5.66%)	
occurrences (all)	0	3	
Renal and urinary disorders			
Urinary tract infection			
subjects affected / exposed	7 / 107 (6.54%)	5 / 53 (9.43%)	
occurrences (all)	12	9	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	6 / 107 (5.61%)	3 / 53 (5.66%)	
occurrences (all)	10	3	
Arthralgia			
subjects affected / exposed	5 / 107 (4.67%)	2 / 53 (3.77%)	
occurrences (all)	5	3	
Muscle cramping			
subjects affected / exposed	5 / 107 (4.67%)	1 / 53 (1.89%)	
occurrences (all)	5	1	
Infections and infestations			
Common cold			
subjects affected / exposed	4 / 107 (3.74%)	4 / 53 (7.55%)	
occurrences (all)	6	5	

Fever			
subjects affected / exposed	4 / 107 (3.74%)	4 / 53 (7.55%)	
occurrences (all)	4	5	
Metabolism and nutrition disorders			
Hypokalemia			
subjects affected / exposed	12 / 107 (11.21%)	5 / 53 (9.43%)	
occurrences (all)	19	15	
Anorexia			
subjects affected / exposed	18 / 107 (16.82%)	9 / 53 (16.98%)	
occurrences (all)	18	10	
Dysgeusia			
subjects affected / exposed	5 / 107 (4.67%)	7 / 53 (13.21%)	
occurrences (all)	5	10	
Hypomagnesaemia			
subjects affected / exposed	5 / 107 (4.67%)	2 / 53 (3.77%)	
occurrences (all)	6	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 December 2016	Update inclusion and exclusion criteria, physician's choice chemotherapy options and protocol assessments

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported