Clinical trial results:
Pazopanib with 5-Flourouracil, Leucovorin and Oxaliplatin (FLO) as 1st-line treatment in advanced gastric cancer; a randomized Phase II study. - The PaFLO study.

Summary

EudraCT number	2010-024379-15
Trial protocol	DE
Global end of trial date	19 November 2015

Results information

Result version number	v1 (current)
This version publication date	28 April 2022
First version publication date	28 April 2022

Trial information

Trial identification

Sponsor protocol code	PaFLO

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01503372
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Charité - University Hospital of Berlin
Sponsor organisation address	Augustenburger Platz 1, Berlin, Germany, 13353
Public contact	Dr. Peter Thuß-Patience, Charité - Universitätsmedizin Berlin, 49 30450653193, peter.thuss@charite.de
Scientific contact	Dr. Peter Thuß-Patience, Charité - Universitätsmedizin Berlin, 49 30450653193, peter.thuss@charite.de

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	19 November 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 November 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

progression free survival rate at 6 months

Protection of trial subjects:

Inclusion and exlusion criteria were implemented to protect the patients.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2011
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	Germany: 78
Worldwide total number of subjects	78
EEA total number of subjects	78

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	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients from 20 national clinical centers were included and between December 2011 and July 2014, 87 patients were enrolled.

Pre-assignment

Screening details:

87 Patients were screened
And 9 Patients were excluded.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	PaFLO Group

Arm description:

Medication (FLO) on day one every 2 weeks for 12 cycles and pazopanib once daily

Arm type	Experimental
Investigational medicinal product name	Pazopanib
Investigational medicinal product code	GW786034
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

800mg once a day

Investigational medicinal product name	5-FU
Investigational medicinal product code	5-FU
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

5-FU was administered with 2600 mg/m2 over 24 hours

Investigational medicinal product name	Oxaliplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

oxaliplatin 85 mg/m² over 2 hours on day one every 2 weeks for 12 cycles

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

Dosage and administration details:

leucovorine 200 mg/m² over 2 hours

Arm title	FLO Group
Arm description: Medication on day one every 2 weeks for 12 cycles	
Arm type	Active comparator
Investigational medicinal product name	5-FU
Investigational medicinal product code	5-FU
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 5-FU was administered with 2600 mg/m² over 24 hours	
Investigational medicinal product name	Oxaliplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: oxaliplatin 85 mg/m² over 2 hours	
Investigational medicinal product name	Folinic acid
Investigational medicinal product code	
Other name	Leucovorin
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: leucovorine 200 mg/m² over 2 hours	

Number of subjects in period 1	PaFLO Group	FLO Group
Started	51	27
Completed	51	27

Baseline characteristics

Reporting groups	
Reporting group title	PaFLO Group
Reporting group description:	
Medication (FLO) on day one every 2 weeks for 12 cycles and pazopanib once daily	
Reporting group title	FLO Group
Reporting group description:	
Medication on day one every 2 weeks for 12 cycles	

Reporting group values	PaFLO Group	FLO Group	Total
Number of subjects	51	27	78
Age categorical Units: Subjects			
Adults >= 18	51	27	78
Gender categorical Units: Subjects			
Female	14	10	24
Male	37	17	54
ECOG			
Eastern Cooperative Oncology Group (ECOG) system			
Units: Subjects			
status 0	22	12	34
status 1	26	13	39
status 2	3	2	5
Site of tumor			
AEG, adenocarcinoma of the esophago-gastric junction			
Units: Subjects			
AEG	30	8	38
Stomach	21	19	40
Histological type (Laurén) Units: Subjects			
Intestinal	15	9	24
Diffuse	8	6	14
Mixed	6	1	7
Not specified	19	10	29
N/A	3	1	4
WHO classification Units: Subjects			
Mucinous	1	1	2
Tubular	6	3	9
Signet ring cells	9	8	17
Not specified	26	12	38
N/A	9	3	12
Clinical stage (T), UICC version 7.0 Units: Subjects			
T0	1	0	1
uT1	5	1	6

uT2	3	0	3
uT3	14	11	25
uT4	10	4	14
uT4a	1	1	2
Tx	13	8	21
N/A	4	2	6
Metastatic spread (M), UICC version 7.0 Units: Subjects			
M0	3	0	3
M1	48	27	75
No. organs involved Units: Subjects			
1 Organ	1	2	3
2 Organs	14	11	25
>=3 Organs	36	14	50
Local recurrence Units: Subjects			
Yes	9	5	14
No	42	22	64

End points

End points reporting groups

Reporting group title	PaFLO Group
Reporting group description:	
Medication (FLO) on day one every 2 weeks for 12 cycles and pazopanib once daily	
Reporting group title	FLO Group
Reporting group description:	
Medication on day one every 2 weeks for 12 cycles	

Primary: Progression-free survival during treatment

End point title	Progression-free survival during treatment
End point description:	
For the Kaplan-Meier curve of progression-free survival see attachment PFS curve	
End point type	Primary
End point timeframe:	
at 6 months	

End point values	PaFLO Group	FLO Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	27		
Units: months				
number (not applicable)				
Median FPS	4.66	4.47		

Attachments (see zip file)	PFS curve/PFS.pdf

Statistical analyses

Statistical analysis title	exploratory comparisons
Comparison groups	PaFLO Group v FLO Group
Number of subjects included in analysis	78
Analysis specification	Post-hoc
Analysis type	superiority[1]
P-value	≤ 0.05 [2]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.96

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.55

Notes:

[1] - The FLO arm served as internal control as calibration arm without preplanned comparisons between the two arms. Therefore, all comparisons are of exploratory nature. The estimation of survival rates was performed according to Kaplan-Meier analysis. Statistical comparison analysis applied the log-rank test and the proportional hazard model.
[2] - All tests are two-sided following the 5% level of significance using SPSS 27.0

Primary: The rate of patients without progression at 6 months

End point title	The rate of patients without progression at 6 months

End point description:

The median OS was numerically higher in the PaFLO arm compared to FLO (10.19 months vs 7.33 months). Despite these promising signs of efficacy of adding pazopanib, when comparing other efficacy parameters to the internal control arm this benefit seems to be small.

End point type	Primary

End point timeframe:

At 6 months

End point values	PaFLO Group	FLO Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	27		
Units: percent				
number (not applicable)				
PFS rate	34	30		

Statistical analyses

Statistical analysis title	Effectivity and tolerability

Statistical analysis description:

The FLO arm served as internal control as calibration arm without preplanned comparisons between the two arms. Therefore, all comparisons are of exploratory nature. The estimation of survival rates was performed according to Kaplan-Meier analysis.

Comparison groups	PaFLO Group v FLO Group
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 [3]
Method	Logrank

Notes:

[3] - All tests are two-sided following the 5% level of significance using SPSS 27.0

Secondary: Overall survival during treatment

End point title	Overall survival during treatment

End point description:

End point type	Secondary

End point timeframe:

6-12 months

End point values	PaFLO Group	FLO Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	27		
Units: months				
number (not applicable)				
Median OS	10.19	7.33		

Statistical analyses

No statistical analyses for this end point

Secondary: Best response confirmed after 12 months

End point title	Best response confirmed after 12 months

End point description:

Abbreviations: CR, complete response; DCR, disease control rate; FLO, 5-fluorouracil, folinic acid, oxaliplatin; ORR, overall response rate; PaFLO, pazopanib plus 5-fluorouracil, folinic acid, oxaliplatin; PR, partial response; SD, stable disease.

End point type	Secondary

End point timeframe:

12 months

End point values	PaFLO Group	FLO Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	27		
Units: Subjects				
CR	1	1		
PR	12	6		
SD	24	9		
PD	9	9		
DCR (CR + PR + SD)	37	16		
ORR (CR + PR)	13	7		

Statistical analyses

No statistical analyses for this end point

Secondary: Toxicity

End point title	Toxicity

End point description:

End point type	Secondary

End point timeframe:

12 months

End point values	PaFLO Group	FLO Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	27		
Units: Subject				
Leucopenia Grade 0	35	24		
Leucopenia Grade 1	4	2		
Leucopenia Grade 2	9	1		
Leucopenia Grade 3	3	0		
Leucopenia Grade 4	0	0		
Neutropenia Grade 0	31	24		
Neutropenia Grade 1	5	2		
Neutropenia Grade 2	3	0		
Neutropenia Grade 3	11	1		
Neutropenia Grade 4	1	0		
Thrombocytopenia Grade 0	36	23		
Thrombocytopenia Grade 1	11	3		
Thrombocytopenia Grade 2	3	1		
Thrombocytopenia Grade 3	1	0		
Thrombocytopenia Grade 4	0	0		
Anemia Grade 0	36	19		
Anemia Grade 1	6	5		
Anemia Grade 2	8	0		
Anemia Grade 3	1	3		
Anemia Grade 4	0	0		
Fever Grade 0	42	25		
Fever Grade 1	5	1		
Fever Grade 2	0	1		
Fever Grade 3	4	0		
Fever Grade 4	0	0		
Nausea Grade 0	16	10		
Nausea Grade 1	19	11		
Nausea Grade 2	8	6		
Nausea Grade 3	8	0		
Nausea Grade 4	0	0		
Loss of appetite Grade 0	23	14		
Loss of appetite Grade 1	17	4		
Loss of appetite Grade 2	6	7		
Loss of appetite Grade 3	4	0		

Loss of appetite Grade 4	0	2		
Vomiting Grade 0	27	15		
Vomiting Grade 1	16	5		
Vomiting Grade 2	5	5		
Vomiting Grade 3	3	2		
Vomiting Grade 4	0	0		
Diarrhea Grade 0	23	16		
Diarrhea Grade 1	21	7		
Diarrhea Grade 2	8	2		
Diarrhea Grade 3	1	2		
Diarrhea Grade 4	0	0		
Obstipation Grade 0	31	20		
Obstipation Grade 1	19	4		
Obstipation Grade 2	1	3		
Obstipation Grade 3	0	0		
Obstipation Grade 4	0	0		
Mucositis Grade 0	39	22		
Mucositis Grade 1	10	4		
Mucositis Grade 2	2	1		
Mucositis Grade 3	0	0		
Mucositis Grade 4	0	0		
Fatigue Grade 0	24	14		
Fatigue Grade 1	15	6		
Fatigue Grade 2	8	6		
Fatigue Grade 3	4	0		
Fatigue Grade 4	0	1		
Alopecia Grade 0	33	22		
Alopecia Grade 1	13	3		
Alopecia Grade 2	0	1		
Alopecia Grade 3	0	1		
Alopecia Grade 4	0	0		
Alteration of nails Grade 0	43	26		
Alteration of nails Grade 1	8	1		
Alteration of nails Grade 2	0	0		
Alteration of nails Grade 3	0	0		
Alteration of nails Grade 4	0	0		
Hand-foot syndrome Grade 0	40	25		
Hand-foot syndrome Grade 1	8	2		
Hand-foot syndrome Grade 2	2	0		
Hand-foot syndrome Grade 3	1	0		
Hand-foot syndrome Grade 4	0	0		
Change in taste Grade 0	34	23		
Change in taste Grade 1	13	3		
Change in taste Grade 2	4	1		
Change in taste Grade 3	0	0		
Change in taste Grade 4	0	0		
Vision disorders Grade 0	45	24		
Vision disorders Grade 1	5	2		
Vision disorders Grade 2	1	1		
Vision disorders Grade 3	0	0		
Vision disorders Grade 4	0	0		
Hearing impairment Grade 0	49	27		

Hearing impairment Grade 1	2	0		
Hearing impairment Grade 2	0	0		
Hearing impairment Grade 3	0	0		
Hearing impairment Grade 4	0	0		
Peripheral neuropathy Grade 0	13	9		
Peripheral neuropathy Grade 1	22	9		
Peripheral neuropathy Grade 2	12	7		
Peripheral neuropathy Grade 3	3	2		
Peripheral neuropathy Grade 4	1	0		
Vertigo Grade 0	41	24		
Vertigo Grade 1	7	2		
Vertigo Grade 2	3	1		
Vertigo Grade 3	0	0		
Vertigo Grade 4	0	0		
ALT Grade 0	42	26		
ALT Grade 1	3	1		
ALT Grade 2	1	0		
ALT Grade 3	5	0		
ALT Grade 4	0	0		
AST Grade 0	43	25		
AST Grade 1	3	2		
AST Grade 2	1	0		
AST Grade 3	4	0		
AST Grade 4	0	0		
Increase of creatinine Grade 0	49	26		
Increase of creatinine Grade 1	2	1		
Increase of creatinine Grade 2	0	0		
Increase of creatinine Grade 3	0	0		
Increase of creatinine Grade 4	0	0		
Bilirubin direct Grade 0	42	23		
Bilirubin direct Grade 1	2	0		
Bilirubin direct Grade 2	0	0		
Bilirubin direct Grade 3	1	0		
Bilirubin direct Grade 4	0	0		
Bilirubin total Grade 0	47	27		
Bilirubin total Grade 1	1	0		
Bilirubin total Grade 2	1	0		
Bilirubin total Grade 3	2	0		
Bilirubin total Grade 4	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Patients with PFS at 9 and 12 months

End point title	Patients with PFS at 9 and 12 months

End point description:

PFS:The length of time during and after the treatment of a disease, such as cancer, that a patient lives with the disease but it does not get worse. In a clinical trial, measuring the progression-free survival is one way to see how well a new treatment works.

End point type	Secondary

End point timeframe:

6 to 9 months

End point values	PaFLO Group	FLO Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	27		
Units: percent				
number (not applicable)				
After 9 months	27	18		
After 12 months	4	7		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
12 months	
Adverse event reporting additional description:	
non-serious AEs were Grade 1 and 2 serious AE were Grade 3 and 4	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups	
Reporting group title	PaFLO
Reporting group description: -	
Reporting group title	FLO-Group
Reporting group description: -	

Serious adverse events	PaFLO	FLO-Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 51 (23.53%)	3 / 27 (11.11%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
ALT	Additional description: Alanin-Amino-Transferase		
subjects affected / exposed	5 / 51 (9.80%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
AST	Additional description: Aspartat-AminoTransferase		
subjects affected / exposed	4 / 51 (7.84%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bilirubin direct			
subjects affected / exposed	1 / 51 (1.96%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bilirubin total			

subjects affected / exposed	2 / 51 (3.92%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Peripheral neuropathy			
subjects affected / exposed	4 / 51 (7.84%)	2 / 27 (7.41%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Leucopenia			
subjects affected / exposed	3 / 51 (5.88%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	12 / 51 (23.53%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 12	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 51 (1.96%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anemia			
subjects affected / exposed	1 / 51 (1.96%)	3 / 27 (11.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Fever			
subjects affected / exposed	4 / 51 (7.84%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
nausea			
subjects affected / exposed	8 / 51 (15.69%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	0 / 8	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Diarrhea			
subjects affected / exposed	1 / 51 (1.96%)	2 / 27 (7.41%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	4 / 51 (7.84%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 51 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand-foot syndrome			
subjects affected / exposed	1 / 51 (1.96%)	0 / 27 (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			
Loss of appetite			
subjects affected / exposed	5 / 51 (9.80%)	2 / 27 (7.41%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	3 / 51 (5.88%)	2 / 27 (7.41%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	PaFLO	FLO-Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	51 / 51 (100.00%)	27 / 27 (100.00%)	
Investigations			
ALT	Additional description: Alanin-Amino-Transferase		

subjects affected / exposed	4 / 51 (7.84%)	1 / 27 (3.70%)	
occurrences (all)	4	1	
AST	Additional description: Aspartat-AminoTransferase		
subjects affected / exposed	4 / 51 (7.84%)	2 / 27 (7.41%)	
occurrences (all)	4	2	
Increase of creatinine			
subjects affected / exposed	2 / 51 (3.92%)	1 / 27 (3.70%)	
occurrences (all)	2	1	
Bilirubin direct			
subjects affected / exposed	2 / 51 (3.92%)	1 / 27 (3.70%)	
occurrences (all)	2	1	
Bilirubin total			
subjects affected / exposed	2 / 51 (3.92%)	0 / 27 (0.00%)	
occurrences (all)	2	0	
Nervous system disorders			
Change in taste			
subjects affected / exposed	17 / 51 (33.33%)	4 / 27 (14.81%)	
occurrences (all)	17	4	
Peripheral neuropathy			
subjects affected / exposed	34 / 51 (66.67%)	16 / 27 (59.26%)	
occurrences (all)	34	16	
Blood and lymphatic system disorders			
Leucopenia			
subjects affected / exposed	13 / 51 (25.49%)	3 / 27 (11.11%)	
occurrences (all)	13	3	
Neutropenia			
subjects affected / exposed	8 / 51 (15.69%)	2 / 27 (7.41%)	
occurrences (all)	8	2	
Thrombocytopenia			
subjects affected / exposed	14 / 51 (27.45%)	4 / 27 (14.81%)	
occurrences (all)	14	4	
Anemia			
subjects affected / exposed	14 / 51 (27.45%)	5 / 27 (18.52%)	
occurrences (all)	14	5	
General disorders and administration site conditions			

Fever			
subjects affected / exposed	5 / 51 (9.80%)	2 / 27 (7.41%)	
occurrences (all)	5	2	
Nausea			
subjects affected / exposed	27 / 51 (52.94%)	17 / 27 (62.96%)	
occurrences (all)	27	17	
Mucositis			
subjects affected / exposed	12 / 51 (23.53%)	5 / 27 (18.52%)	
occurrences (all)	12	5	
Fatigue			
subjects affected / exposed	23 / 51 (45.10%)	12 / 27 (44.44%)	
occurrences (all)	23	12	
Alteration of nails			
subjects affected / exposed	8 / 51 (15.69%)	1 / 27 (3.70%)	
occurrences (all)	8	1	
Ear and labyrinth disorders			
Hearing impairment			
subjects affected / exposed	2 / 51 (3.92%)	0 / 27 (0.00%)	
occurrences (all)	2	0	
Vertigo			
subjects affected / exposed	10 / 51 (19.61%)	3 / 27 (11.11%)	
occurrences (all)	10	3	
Eye disorders			
Vision disorders			
subjects affected / exposed	6 / 51 (11.76%)	3 / 27 (11.11%)	
occurrences (all)	6	3	
Gastrointestinal disorders			
Diarrhea			
subjects affected / exposed	29 / 51 (56.86%)	9 / 27 (33.33%)	
occurrences (all)	29	9	
Obstipation			
subjects affected / exposed	20 / 51 (39.22%)	7 / 27 (25.93%)	
occurrences (all)	20	7	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	18 / 51 (35.29%)	4 / 27 (14.81%)	
occurrences (all)	18	4	

Hand-foot syndrome subjects affected / exposed occurrences (all)	10 / 51 (19.61%) 10	2 / 27 (7.41%) 2	
Metabolism and nutrition disorders Loss of appetite subjects affected / exposed occurrences (all)	23 / 51 (45.10%) 23	11 / 27 (40.74%) 11	
Vomiting subjects affected / exposed occurrences (all)	21 / 51 (41.18%) 21	10 / 27 (37.04%) 10	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/34741530