



Clinical trial results:

NeoOn – Neoadjuvant treatment of Ontruzant® (SB3) in patients with HER2-positive early breast cancer: An open-label, multicenter, phase IV study

Summary

EudraCT number	2020-001943-21
Trial protocol	DE
Global end of trial date	23 January 2024

Results information

Result version number	v1 (current)
This version publication date	27 June 2025
First version publication date	27 June 2025
Summary attachment (see zip file)	CSR Synopsis (NeoOn_CSR_Synopsis_Final _2025-01-22_Synopsis.pdf)

Trial information

Trial identification

Sponsor protocol code	IFG-08-2019
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05036005
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Institut für Frauengesundheit GmbH
Sponsor organisation address	Universitätsstraße 21-23, Erlangen, Germany, 91054
Public contact	Clinical Trials Information, Institut für Frauengesundheit, 0049 91319278968, neo.on@ifg-erlangen.de
Scientific contact	Clinical Trials Information, Institut für Frauengesundheit, 0049 91319278968, neo.on@ifg-erlangen.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	22 July 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 January 2024
Global end of trial reached?	Yes
Global end of trial date	23 January 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Pathological complete response (pCR) rate, defined as the complete absence of tumor cells (ypT0; ypN0) after neoadjuvant study treatment of HER2-positive early breast cancer patients treated with Ontruzant® (SB3).

Protection of trial subjects:

The clinical trial was conducted in accordance with current ethical standards, the Declaration of Helsinki from 1996 and the Guidelines of the International Conference on Harmonization Good Clinical Practice (GCP).

Background therapy:

Anthracyclin-free chemotherapy (6 cycles) or sequential anthracycline-taxane based chemotherapy (4 + 4 cycles) according to investigator's discretion and local in-house standard.

Evidence for comparator:

n/a

Actual start date of recruitment	12 July 2021
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	Germany: 99
Worldwide total number of subjects	99
EEA total number of subjects	99

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)	79

From 65 to 84 years	20
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited between 12-Jul-2021 and 15-May-2023 in 3 main trial sites in Germany. The date of last patient last visit was 23-Jan-2024. The database cut was on 22-Jul-2024.

Pre-assignment

Screening details:

Screening was conducted during clinical routine. A total of 103 patients signed the informed consent form and were enrolled in the NeoOn clinical trial. 1 patient was an erroneous entry to the eCRF and was not regarded for the study.

Four patients were identified as screening-failures and did not start trial treatment.

Period 1

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

Blinding implementation details:

open-label, blinding is not applicable

Arms

Arm title	6 cycles of SB3+CTX
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Arm description:

6 cycles of SB3+CTX

Arm type	Experimental
Investigational medicinal product name	Ontruzant
Investigational medicinal product code	SB3
Other name	Trastuzumab Biosimilar
Pharmaceutical forms	Powder for concentrate and solution for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients on an anthracycline-free treatment regimen received an initial dose of Ontruzant® i.v. 8 mg/kg b.w in combination with standard chemotherapy followed by 5 cycles of Ontruzant® i.v. 6 mg/kg b.w. q21d in combination with standard chemotherapy.

Patients on a sequential anthracycline-taxane based treatment regimen received 4 cycles of anthracycline based chemotherapy followed by an initial dose of Ontruzant® i.v. 8 mg/kg b.w in combination with standard taxane based chemotherapy followed by 3 cycles of Ontruzant® i.v. 6 mg/kg b.w. q21d in combination with standard chemotherapy.

Number of subjects in period 1	6 cycles of SB3+CTX
Started	99
Completed	99

Baseline characteristics

Reporting groups

Reporting group title	Overall period
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Reporting group description: -

Reporting group values	Overall period	Total	
Number of subjects	99	99	
Age categorical			
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	
Age continuous			
Units: years			
arithmetic mean	52.8		
standard deviation	± 12.2	-	
Gender categorical			
Units: Subjects			
Female	99	99	
Male	0	0	
Ethnicity			
Units: Subjects			
Caucasian	94	94	
Other	3	3	
Missing	2	2	
ECOG			
Units: Subjects			
ECOG 0	95	95	
ECOG 1	4	4	
ECOG 2	0	0	
ECOG 3	0	0	
ECOG 4	0	0	
Missing	0	0	
Menopausal state			
Units: Subjects			
Pre-/ perimenopausal	49	49	
Postmenopausal	50	50	
Missing	0	0	
Tumor stage			
Units: Subjects			

cT1	36	36	
cT2	47	47	
cT3	7	7	
cT4	7	7	
cTx	2	2	
Missing	0	0	
Lymph node status Units: Subjects			
cN0	49	49	
cN1-3	41	41	
cNx	9	9	
Missing	0	0	
Previous lymph node procedure Units: Subjects			
yes	26	26	
no	71	71	
missing	2	2	
Pathological lymph node status Units: Subjects			
pN0	0	0	
pNx	5	5	
pN1-3	12	12	
missing	82	82	
cM Units: Subjects			
cM0	90	90	
cMx	9	9	
missing	0	0	
Grading Units: Subjects			
G1	3	3	
G2	37	37	
G3	57	57	
missing	2	2	
Histological subtype Units: Subjects			
ductal	84	84	
lobular	7	7	
mixed ductal/ lobular	0	0	
other	4	4	
missing	4	4	
ER status Units: Subjects			
ER+	66	66	
ER	32	32	
missing	1	1	
PgR status Units: Subjects			
PgR+	52	52	
PgR-	46	46	
missing	1	1	

HER2 status Units: Subjects			
HER2+	98	98	
HER2-	0	0	
missing	1	1	
Concomitant diseases Units: Subjects			
yes	69	69	
no	30	30	
missing	0	0	
Planned treatment regimen Units: Subjects			
6x SB3 + CTX	0	0	
6x SB3+CTX + PZM	99	99	
4x CTX-A – 4xCTX-T + SB3	0	0	
4x CTX-A – 4xCTX-T + SB3 + PZM	0	0	
missing	0	0	
Platin-based chemotherapy Units: Subjects			
Carboplatin	99	99	
other	0	0	
missing	0	0	
Taxane-based chemotherapy Units: Subjects			
Pacitaxel	82	82	
nab-Paclitaxel	0	0	
Docetaxel	17	17	
Other	0	0	
Missing	0	0	
BMI Units: kg/m ³			
arithmetic mean	25.6		
standard deviation	± 5.5	-	
Time from primary diagnosis to therapy begin Units: day			
arithmetic mean	30.9		
standard deviation	± 13.5	-	
Age Units: year			
median	55.0		
inter-quartile range (Q1-Q3)	42.0 to 61.5	-	
BMI Units: kg/m ³			
median	23.8		
inter-quartile range (Q1-Q3)	22.2 to 28.3	-	

Subject analysis sets

Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

The full analysis set (FAS) or efficacy population included all patients meeting the in- and exclusion criteria enrolled into the NeoOn clinical trial who have received at least one full cycle of trial treatment (SB3+CTX or SB3+CTX-T). The full analysis set is also the safety analysis set.

Subject analysis set title	Per Protocol Set
Subject analysis set type	Per protocol

Subject analysis set description:

The per protocol set (PPS) or efficacy population included all patients meeting the in- and exclusion criteria enrolled into the NeoOn clinical trial who have received full 6 cycles of SB3+CTX or 4 cycles SB3+CTX-T, depending on treatment schedule.

Reporting group values	Full Analysis Set	Per Protocol Set	
Number of subjects	99	91	
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	52.8	52.2	
standard deviation	± 12.2	± 11.9	
Gender categorical Units: Subjects			
Female	99	91	
Male	0	0	
Ethnicity Units: Subjects			
Caucasian	94	86	
Other	3	3	
Missing	2	2	
ECOG Units: Subjects			
ECOG 0	95	89	
ECOG 1	4	2	
ECOG 2	0	0	
ECOG 3	0	0	
ECOG 4	0	0	
Missing	0	0	
Menopausal state Units: Subjects			
Pre-/ perimenopausal	49	47	
Postmenopausal	50	44	
Missing	0	0	
Tumor stage			

Units: Subjects			
cT1	36	34	
cT2	47	44	
cT3	7	5	
cT4	7	7	
cTx	2	1	
Missing	0	0	
Lymph node status			
Units: Subjects			
cN0	49	45	
cN1-3	41	38	
cNx	9	8	
Missing	0	0	
Previous lymph node procedure			
Units: Subjects			
yes	26	23	
no	71	66	
missing	2	2	
Pathological lymph node status			
Units: Subjects			
pN0	0	0	
pNx	5	5	
pN1-3	12	11	
missing	82	75	
cM			
Units: Subjects			
cM0	90	82	
cMx	9	9	
missing	0	0	
Grading			
Units: Subjects			
G1	3	3	
G2	37	34	
G3	57	52	
missing	2	2	
Histological subtype			
Units: Subjects			
ductal	84	77	
lobular	7	6	
mixed ductal/ lobular	0	0	
other	4	4	
missing	4	4	
ER status			
Units: Subjects			
ER+	66	60	
ER	32	30	
missing	1	1	
PgR status			
Units: Subjects			
PgR+	52	48	
PgR-	46	42	

missing	1	1	
HER2 status			
Units: Subjects			
HER2+	98	90	
HER2-	0	0	
missing	1	1	
Concomitant diseases			
Units: Subjects			
yes	69	62	
no	30	29	
missing	0	0	
Planned treatment regimen			
Units: Subjects			
6x SB3 + CTX	0	0	
6x SB3+CTX + PZM	99	91	
4x CTX-A - 4xCTX-T + SB3	0	0	
4x CTX-A - 4xCTX-T + SB3 + PZM	0	0	
missing	0	0	
Platin-based chemotherapy			
Units: Subjects			
Carboplatin	99	91	
other	0	0	
missing	0	0	
Taxane-based chemotherapy			
Units: Subjects			
Pacitaxel	82	78	
nab-Paclitaxel	0	0	
Docetaxel	17	13	
Other	0	0	
Missing	0	0	
BMI			
Units: kg/m ³			
arithmetic mean	25.6	25.4	
standard deviation	± 5.5	± 5.6	
Time from primary diagnosis to therapy begin			
Units: day			
arithmetic mean	30.9	30.5	
standard deviation	± 13.5	± 13.6	
Age			
Units: year			
median	55.0	55.0	
inter-quartile range (Q1-Q3)	42.0 to 61.5	42.0 to 60.5	
BMI			
Units: kg/m ³			
median	23.8	23.7	
inter-quartile range (Q1-Q3)	22.2 to 28.3	21.9 to 27.7	

End points

End points reporting groups

Reporting group title	6 cycles of SB3+CTX
Reporting group description: 6 cycles of SB3+CTX	
Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis
Subject analysis set description: The full analysis set (FAS) or efficacy population included all patients meeting the in- and exclusion criteria enrolled into the NeoOn clinical trial who have received at least one full cycle of trial treatment (SB3+CTX or SB3+CTX-T). The full analysis set is also the safety analysis set.	
Subject analysis set title	Per Protocol Set
Subject analysis set type	Per protocol
Subject analysis set description: The per protocol set (PPS) or efficacy population included all patients meeting the in- and exclusion criteria enrolled into the NeoOn clinical trial who have received full 6 cycles of SB3+CTX or 4 cycles SB3+CTX-T, depending on treatment schedule.	

Primary: pCR rate (ypT0 and ypN0)

End point title	pCR rate (ypT0 and ypN0)
End point description: pCR, ypT0 and ypN0	
End point type	Primary
End point timeframe: End of treatment/ surgery	

End point values	6 cycles of SB3+CTX	Full Analysis Set	Per Protocol Set	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	99	99	91	
Units: patients				
pCR	57	57	53	
no pCR	39	39	37	
missing	3	3	1	

Statistical analyses

Statistical analysis title	pCR rate
Statistical analysis description: one-sided binomial test testing the null hypothesis that the pCR rate is at most 30%	
Comparison groups	6 cycles of SB3+CTX v Full Analysis Set v Per Protocol Set

Number of subjects included in analysis	289
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.000001
Method	binomial test
Confidence interval	
level	95 %
sides	2-sided
lower limit	48.9
upper limit	69.3

Secondary: pCR (ypT0/is and ypN0)

End point title	pCR (ypT0/is and ypN0)
End point description: pCR (ypT0/is and ypN0)	
End point type	Secondary
End point timeframe: Surgery/ end of treatment	

End point values	6 cycles of SB3+CTX	Full Analysis Set	Per Protocol Set	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	99	99	91	
Units: patients				
pCR	57	57	53	
no pCR	39	39	37	
missing	3	3	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical response end of treatment

End point title	Clinical response end of treatment
End point description:	
End point type	Secondary
End point timeframe: End of treatment	

End point values	6 cycles of SB3+CTX	Full Analysis Set	Per Protocol Set	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	99	99	91	
Units: patients				
Complete response	26	26	23	
Partial response	58	58	56	
Progressive disease	5	5	5	
Stable disease	5	5	5	
Missing	5	5	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Best overall response

End point title	Best overall response
End point description:	
End point type	Secondary
End point timeframe:	
End of Treatment	

End point values	6 cycles of SB3+CTX	Full Analysis Set	Per Protocol Set	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	99	99	91	
Units: patients				
Complete response	26	26	23	
Partial response	62	62	60	
Progressive disease	0	0	0	
Stable disease	6	6	6	
Missing	5	5	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Global Health

End point title	Global Health
End point description:	
Global health subscale according to EORTC-QLQ-C30	
End point type	Secondary

End point timeframe:
Baseline - End of study

End point values	6 cycles of SB3+CTX	Full Analysis Set	Per Protocol Set	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	99	99	91	
Units: score on scale				
arithmetic mean (standard deviation)				
1. CTX-SB3/ 1. CTXA	68.3 (± 20.1)	68.3 (± 20.1)	68.6 (± 20)	
4. CTX-SB3/ 1. CTXT-SB3	54.6 (± 20.5)	54.6 (± 20.5)	55.1 (± 20.3)	
EoT/Surgery	54.0 (± 20.5)	54.0 (± 20.5)	53.9 (± 21.0)	
Safety-FU	61.0 (± 20.1)	61.0 (± 20.1)	61.4 (± 19.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Physical Functioning

End point title	Physical Functioning
End point description:	
Physical Functioning subscale according to EORTC-QLQ-C30	
End point type	Secondary
End point timeframe:	
Baseline - End of study	

End point values	6 cycles of SB3+CTX	Full Analysis Set	Per Protocol Set	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	99	99	91	
Units: score on scale				
arithmetic mean (standard deviation)				
1. CTX-SB3/ 1. CTXA	90.1 (± 14.2)	90.1 (± 14.2)	91.0 (± 13.7)	
4. CTX-SB3/ 1. CTXT-SB3	68.2 (± 25.0)	68.2 (± 25.0)	70.1 (± 24.1)	
EoT/Surgery	66.1 (± 24.7)	66.1 (± 24.7)	67.3 (± 24.0)	
Safety-FU	75.5 (± 24.2)	75.5 (± 24.2)	76.6 (± 23.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Role Functioning

End point title	Role Functioning
End point description: RoleFunctioning subscale according to EORTC-QLQ-C30	
End point type	Secondary
End point timeframe: Baseline - End of study	

End point values	6 cycles of SB3+CTX	Full Analysis Set	Per Protocol Set	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	99			
Units: score on scale				
arithmetic mean (standard deviation)				
1. CTX-SB3/ 1. CTXA	80.9 (± 25.9)	80.9 (± 25.9)	81.5 (± 25.2)	
4. CTX-SB3/ 1. CTXT-SB3	52.2 (± 32.2)	52.2 (± 32.2)	54.2 (± 32.0)	
EoT/Surgery	52.2 (± 31.3)	52.2 (± 31.3)	52.8 (± 31.6)	
Safety-FU	56.0 (± 31.7)	56.0 (± 31.7)	56.4 (± 31.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Emotional Functioning

End point title	Emotional Functioning
End point description: Emoional Functioning subscale according to EORTC-QLQ-C30	
End point type	Secondary
End point timeframe: Baseline- End of study	

End point values	6 cycles of SB3+CTX	Full Analysis Set	Per Protocol Set	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	99	99	91	
Units: score on scale				
arithmetic mean (standard deviation)				
1. CTX-SB3/ 1. CTXA	58.9 (± 26.8)	58.9 (± 26.8)	58.9 (± 26.8)	
4. CTX-SB3/ 1. CTXT-SB3	64.3 (± 26.1)	64.3 (± 26.1)	64.3 (± 26.1)	
EoT/Surgery	62.3 (± 23.6)	62.3 (± 23.6)	62.3 (± 23.6)	
Safety-FU	66.6 (± 23.4)	66.6 (± 23.4)	66.6 (± 23.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Cognitive Functioning

End point title Cognitive Functioning

End point description:

Cognitive Functioning subscale according to EORTC-QLQ-C30

End point type Secondary

End point timeframe:

Baseline - End of Study

End point values	6 cycles of SB3+CTX	Full Analysis Set	Per Protocol Set	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	99	99	91	
Units: score on scale				
arithmetic mean (standard deviation)				
1. CTX-SB3/ 1. CTXA	86.9 (± 19.3)	86.9 (± 19.3)	88.7 (± 17.1)	
4. CTX-SB3/ 1. CTXT-SB3	71.7 (± 25.3)	71.7 (± 25.3)	72.4 (± 25.6)	
EoT/Surgery	73.1 (± 23.4)	73.1 (± 23.4)	73.1 (± 22.9)	
Safety-FU	75.0 (± 26.9)	75.0 (± 26.9)	74.3 (± 27.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Social Functioning

End point title Social Functioning

End point description:

Social Functioning subscale according to EORTC-QLQ-C30

End point type Secondary

End point timeframe:

Baseline - End of study

End point values	6 cycles of SB3+CTX	Full Analysis Set	Per Protocol Set	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	99	99	91	
Units: score on scale				
arithmetic mean (standard deviation)				
1. CTX-SB3/ 1. CTXA	71.3 (± 27.1)	71.3 (± 27.1)	72.0 (± 25.7)	
4. CTX-SB3/ 1. CTXT-SB3	55.8 (± 31.2)	55.8 (± 31.2)	56.6 (± 31.4)	
EoT/Surgery	56.3 (± 30.5)	56.3 (± 30.5)	56.9 (± 30.8)	

Safety-FU	64.0 (± 29.8)	64.0 (± 29.8)	64.0 (± 30.3)	
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Statistical analyses

No statistical analyses for this end point

Secondary: Fatigue

End point title	Fatigue
End point description:	
Fatigue subscale according to EORTC-QLQ-C30	
End point type	Secondary
End point timeframe:	
Baseline - End of study	

End point values	6 cycles of SB3+CTX	Full Analysis Set	Per Protocol Set	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	99	99	91	
Units: score on scale				
arithmetic mean (standard deviation)				
1. CTX-SB3/ 1. CTXA	23.7 (± 24.2)	23.7 (± 24.2)	23.3 (± 24.5)	
4. CTX-SB3/ 1. CTXT-SB3	54.0 (± 29.7)	54.0 (± 29.7)	52.7 (± 29.8)	
EoT/Surgery	50.8 (± 28.5)	50.8 (± 28.5)	50.1 (± 28.7)	
Safety-FU	42.9 (± 30.3)	42.9 (± 30.3)	42.4 (± 30.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Nausea and vomiting

End point title	Nausea and vomiting
End point description:	
Nausea and vomiting subscale according to EORTC-QLQ-C30	
End point type	Secondary
End point timeframe:	
Baseline - End of study	

End point values	6 cycles of SB3+CTX	Full Analysis Set	Per Protocol Set	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	99	99	91	
Units: score on scale				
arithmetic mean (standard deviation)				
1. CTX-SB3/ 1. CTXA	3.8 (± 11.7)	3.8 (± 11.7)	4.0 (± 12.2)	
4. CTX-SB3/ 1. CTXT-SB3	20.8 (± 24.3)	20.8 (± 24.3)	19.8 (± 23.9)	
EoT/Surgery	13.5 (± 21.9)	13.5 (± 21.9)	50.1 (± 28.7)	
Safety-FU	8.3 (± 15.7)	8.3 (± 15.7)	42.4 (± 33.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Pain

End point title	Pain
End point description:	
Pain subscale according to EORTC-QLQ-C30	
End point type	Secondary
End point timeframe:	
Baseline - End of study	

End point values	6 cycles of SB3+CTX	Full Analysis Set	Per Protocol Set	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	99	99	91	
Units: score on scale				
arithmetic mean (standard deviation)				
1. CTX-SB3/ 1. CTXA	18.1 (± 23.0)	18.1 (± 23.0)	18.0 (± 23.2)	
4. CTX-SB3/ 1. CTXT-SB3	26.2 (± 29.2)	26.2 (± 29.2)	23.6 (± 27.6)	
EoT/Surgery	28.6 (± 29.9)	28.6 (± 29.9)	28.3 (± 30.3)	
Safety-FU	30.0 (± 32.6)	30.0 (± 32.6)	30.5 (± 33.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Dyspnea

End point title	Dyspnea
End point description:	
Dyspnoe subscale according to EORTC-QLQ-C30	
End point type	Secondary

End point timeframe:
Baseline - End of study

End point values	6 cycles of SB3+CTX	Full Analysis Set	Per Protocol Set	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	99	99	91	
Units: score on scale				
arithmetic mean (standard deviation)				
1. CTX-SB3/ 1. CTXA	9.6 (± 18.4)	9.6 (± 18.4)	8.4 (± 16.5)	
4. CTX-SB3/ 1. CTXT-SB3	43.3 (± 33.4)	43.3 (± 33.4)	42.6 (± 33.3)	
EoT/Surgery	42.0 (± 31.4)	42.0 (± 31.4)	43.3 (± 31.1)	
Safety-FU	27.9 (± 29.3)	27.9 (± 29.3)	27.6 (± 29.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Insomnia

End point title	Insomnia
End point description: Insomnia subscale according to EORTC-QLQ-C30	
End point type	Secondary
End point timeframe: Baseline - End of study	

End point values	6 cycles of SB3+CTX	Full Analysis Set	Per Protocol Set	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	99	99	91	
Units: score on scale				
arithmetic mean (standard deviation)				
1. CTX-SB3/ 1. CTXA	34.1 (± 31.7)	34.1 (± 31.7)	34.2 (± 31.9)	
4. CTX-SB3/ 1. CTXT-SB3	49.2 (± 34.1)	49.2 (± 34.1)	48.1 (± 34.1)	
EoT/Surgery	45.1 (± 30.7)	45.1 (± 30.7)	44.6 (± 30.9)	
Safety-FU	43.3 (± 32.0)	43.3 (± 32.0)	43.4 (± 32.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Appetite loss

End point title	Appetite loss
End point description: Appetite loss subscale according to EORTC-QLQ-C30	
End point type	Secondary
End point timeframe: Baseline - End of study	

End point values	6 cycles of SB3+CTX	Full Analysis Set	Per Protocol Set	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	99	99	91	
Units: score on scale				
arithmetic mean (standard deviation)				
1. CTX-SB3/ 1. CTXA	18.1 (± 25.7)	18.1 (± 25.7)	18.2 (± 26.4)	
4. CTX-SB3/ 1. CTXT-SB3	36.5 (± 34.9)	36.5 (± 34.9)	35.0 (± 35.0)	
EoT/Surgery	28.6 (± 33.0)	28.6 (± 33.0)	27.1 (± 32.3)	
Safety-FU	19.6 (± 28.4)	19.6 (± 28.4)	18.4 (± 28.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Constipation

End point title	Constipation
End point description: Constipation subscale according to EORTC-QLQ-C30	
End point type	Secondary
End point timeframe: Baseline - End of study	

End point values	6 cycles of SB3+CTX	Full Analysis Set	Per Protocol Set	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	99	99	91	
Units: score on scale				
arithmetic mean (standard deviation)				
1. CTX-SB3/ 1. CTXA	8.8 (± 23.3)	8.8 (± 23.3)	9.8 (± 24.4)	
4. CTX-SB3/ 1. CTXT-SB3	16.3 (± 27.1)	16.3 (± 27.1)	16.5 (± 27.7)	
EoT/Surgery	9.8 (± 20.5)	9.8 (± 20.5)	9.2 (± 19.8)	
Safety-FU	9.2 (± 19.8)	9.2 (± 19.8)	8.3 (± 17.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Diarrhea

End point title Diarrhea

End point description:

Diarrhea subscale according to EORTC-QLQ-C30

End point type Secondary

End point timeframe:

Baseline - End of study

End point values	6 cycles of SB3+CTX	Full Analysis Set	Per Protocol Set	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	99	99	91	
Units: score on scale				
arithmetic mean (standard deviation)				
1. CTX-SB3/ 1. CTXA	10.0 (± 17.8)	10.0 (± 17.8)	10.2 (± 18.2)	
4. CTX-SB3/ 1. CTXT-SB3	52.0 (± 33.3)	52.0 (± 33.3)	53.2 (± 32.3)	
EoT/Surgery	39.6 (± 35.8)	39.6 (± 35.8)	38.3 (± 35.6)	
Safety-FU	12.5 (± 21.5)	12.5 (± 21.5)	11.8 (± 20.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Financial difficulties

End point title Financial difficulties

End point description:

Financial difficulties subscale according to EORTC-QLQ-C30

End point type Secondary

End point timeframe:

Baseline - End of study

End point values	6 cycles of SB3+CTX	Full Analysis Set	Per Protocol Set	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	99	99	91	
Units: score on scale				
arithmetic mean (standard deviation)				
1. CTX-SB3/ 1. CTXA	11.9 (± 24.3)	11.9 (± 24.3)	12.6 (± 25.1)	
4. CTX-SB3/ 1. CTXT-SB3	18.9 (± 27.6)	18.9 (± 27.6)	17.9 (± 26.7)	
EoT/Surgery	17.3 (± 24.6)	17.3 (± 24.6)	18.4 (± 25.0)	

Safety-FU	18.7 (± 27.5)	18.7 (± 27.5)	19.3 (± 27.9)	
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Statistical analyses

No statistical analyses for this end point

Secondary: Body Image

End point title	Body Image
End point description: Body image subscale according to EORTC-QLQ-BR23	
End point type	Secondary
End point timeframe: Baseline - End of study	

End point values	6 cycles of SB3+CTX	Full Analysis Set	Per Protocol Set	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	99	99	91	
Units: score on scale				
arithmetic mean (standard deviation)				
1. CTX-SB3/ 1. CTXA	85.1 (± 20.5)	85.1 (± 20.5)	85.9 (± 17.8)	
4. CTX-SB3/ 1. CTXT-SB3	61.8 (± 32.5)	61.8 (± 32.5)	61.1 (± 31.9)	
EoT/Surgery	59.9 (± 31.4)	59.9 (± 31.4)	59.1 (± 31.4)	
Safety-FU	64.4 (± 28.0)	64.4 (± 28.0)	64.7 (± 28.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Sexual functioning

End point title	Sexual functioning
End point description: Sexual functioning subscale according to EORTC-QLQ-BR23	
End point type	Secondary
End point timeframe: Baseline - End of study	

End point values	6 cycles of SB3+CTX	Full Analysis Set	Per Protocol Set	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	99	99	91	
Units: score on scale				
arithmetic mean (standard deviation)				
1. CTX-SB3/ 1. CTXA	21.6 (± 24.6)	21.6 (± 24.6)	21.6 (± 24.1)	
4. CTX-SB3/ 1. CTXT-SB3	16.0 (± 23.3)	16.0 (± 23.3)	16.0 (± 23.5)	
EoT/Surgery	11.3 (± 19.2)	11.3 (± 19.2)	11.6 (± 19.5)	
Safety-FU	21.7 (± 28.8)	21.7 (± 28.8)	22.5 (± 29.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Sexual enjoyment

End point title	Sexual enjoyment
End point description:	
Sexual enjoyment subscale according to EORTC-QLQ-BR23	
End point type	Secondary
End point timeframe:	
Baseline - End of study	

End point values	6 cycles of SB3+CTX	Full Analysis Set	Per Protocol Set	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	99	99	91	
Units: score on scale				
arithmetic mean (standard deviation)				
1. CTX-SB3/ 1. CTXA	76.8 (± 29.2)	76.8 (± 29.2)	76.7 (± 28.8)	
4. CTX-SB3/ 1. CTXT-SB3	57.3 (± 32.7)	57.3 (± 32.7)	56.5 (± 32.5)	
EoT/Surgery	54.9 (± 20.2)	54.9 (± 20.2)	54.2 (± 20.6)	
Safety-FU	73.1 (± 26.7)	73.1 (± 26.7)	74.7 (± 26.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Future perspective

End point title	Future perspective
End point description:	
Future perspective subscale according to EORTC-QLQ-BR23	
End point type	Secondary

End point timeframe:
Baseline - End of study

End point values	6 cycles of SB3+CTX	Full Analysis Set	Per Protocol Set	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	99	99	91	
Units: score on scale				
arithmetic mean (standard deviation)				
1. CTX-SB3/ 1. CTXA	31.6 (± 34.8)	31.6 (± 34.8)	32.9 (± 35.0)	
4. CTX-SB3/ 1. CTXT-SB3	44.2 (± 31.7)	44.2 (± 31.7)	44.0 (± 31.6)	
EoT/Surgery	39.0 (± 33.7)	39.0 (± 33.7)	38.0 (± 32.6)	
Safety-FU	47.9 (± 33.4)	47.9 (± 33.4)	47.7 (± 33.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Systemic therapy side effects

End point title	Systemic therapy side effects
End point description: Systemic therapy side effects subscale according to EORTC-QLQ-BR23	
End point type	Secondary
End point timeframe: Baseline - End of study	

End point values	6 cycles of SB3+CTX	Full Analysis Set	Per Protocol Set	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	99	99	91	
Units: score on scale				
arithmetic mean (standard deviation)				
1. CTX-SB3/ 1. CTXA	12.9 (± 12.9)	12.9 (± 12.9)	12.9 (± 13.0)	
4. CTX-SB3/ 1. CTXT-SB3	41.4 (± 17.9)	41.4 (± 17.9)	40.8 (± 18.0)	
EoT/Surgery	36.8 (± 17.7)	36.8 (± 17.7)	36.2 (± 17.5)	
Safety-FU	22.7 (± 14.9)	22.7 (± 14.9)	22.4 (± 15.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Breast symptoms

End point title	Breast symptoms
End point description: Breast symptoms subscale according to EORTC-QLQ-BR23	
End point type	Secondary
End point timeframe: Baseline - End of study	

End point values	6 cycles of SB3+CTX	Full Analysis Set	Per Protocol Set	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	99	99	91	
Units: score on scale				
arithmetic mean (standard deviation)				
1. CTX-SB3/ 1. CTXA	16.9 (± 18.9)	16.9 (± 18.9)	17.2 (± 19.3)	
4. CTX-SB3/ 1. CTXT-SB3	9.9 (± 16.3)	9.9 (± 16.3)	8.8 (± 14.5)	
EoT/Surgery	10.5 (± 14.4)	10.5 (± 14.4)	10.2 (± 14.4)	
Safety-FU	28.0 (± 23.6)	28.0 (± 23.6)	28.6 (± 23.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Arm symptoms

End point title	Arm symptoms
End point description: Arm symptoms subscale according to EORTC-QLQ-BR23	
End point type	Secondary
End point timeframe: Baseline - End of study	

End point values	6 cycles of SB3+CTX	Full Analysis Set	Per Protocol Set	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	99	99	91	
Units: score on scale				
arithmetic mean (standard deviation)				
1. CTX-SB3/ 1. CTXA	15.5 (± 19.8)	15.5 (± 19.8)	15.7 (± 20.0)	
4. CTX-SB3/ 1. CTXT-SB3	11.5 (± 19.4)	11.5 (± 19.4)	10.4 (± 18.3)	
EoT/Surgery	13.3 (± 19.0)	13.3 (± 19.0)	12.2 (± 18.4)	
Safety-FU	24.3 (± 20.6)	24.3 (± 20.6)	24.4 (± 20.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Upset by hair loss

End point title	Upset by hair loss
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End point description:

Upset by hair loss subscale according to EORTC-QLQ-BR23

End point type	Secondary
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End point timeframe:

Baseline - End of study

End point values	6 cycles of SB3+CTX	Full Analysis Set	Per Protocol Set	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	99	99	91	
Units: score on scale				
arithmetic mean (standard deviation)				
1. CTX-SB3/ 1. CTXA	29.6 (± 30.9)	29.6 (± 30.9)	29.6 (± 30.9)	
4. CTX-SB3/ 1. CTXT-SB3	46.3 (± 39.6)	46.3 (± 39.6)	45.2 (± 39.9)	
EoT/Surgery	56.7 (± 38.0)	56.7 (± 38.0)	57.8 (± 38.5)	
Safety-FU	44.4 (± 19.2)	44.4 (± 19.2)	50.0 (± 23.6)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Time of signing ICF until 30 days after cessation of treatment or until last study visit, whichever period is longer.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	22.1
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Reporting groups

Reporting group title	Safety Analysis Set
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Reporting group description:

The safety analysis set (SAS) consisted of all patients who have received at least one dose of trial treatment SB3, regardless of compliance with the trial protocol

Serious adverse events	Safety Analysis Set		
Total subjects affected by serious adverse events			
subjects affected / exposed	26 / 99 (26.26%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Investigations			
Blood potassium decreased			
subjects affected / exposed	4 / 99 (4.04%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Stress cardiomyopathy			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Post stroke seizure			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Syncope			

subjects affected / exposed	1 / 99 (1.01%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	4 / 99 (4.04%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Catheter site inflammation			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chest pain			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General physical health deterioration			
subjects affected / exposed	3 / 99 (3.03%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	7 / 99 (7.07%)		
occurrences causally related to treatment / all	6 / 8		
deaths causally related to treatment / all	0 / 0		
Gastric haemorrhage			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Ileus			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Drug-induced liver injury			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	4 / 99 (4.04%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Catheter site infection			
subjects affected / exposed	3 / 99 (3.03%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Corona virus infection			

subjects affected / exposed	1 / 99 (1.01%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Erysipelas			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Safety Analysis Set		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	99 / 99 (100.00%)		
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Hot flush			

subjects affected / exposed	7 / 99 (7.07%)		
occurrences (all)	7		
Hypertension			
subjects affected / exposed	5 / 99 (5.05%)		
occurrences (all)	6		
Pallor			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Thrombophlebitis superficial			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Venous thrombosis			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Venous thrombosis limb			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
General disorders and administration site conditions			
Catheter site injury			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Chills			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	54 / 99 (54.55%)		
occurrences (all)	73		
Impaired healing			
subjects affected / exposed	3 / 99 (3.03%)		
occurrences (all)	3		
Malaise			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Mucosal dryness			

subjects affected / exposed	3 / 99 (3.03%)		
occurrences (all)	3		
Mucosal toxicity			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Non-cardiac chest pain			
subjects affected / exposed	6 / 99 (6.06%)		
occurrences (all)	7		
Oedema peripheral			
subjects affected / exposed	6 / 99 (6.06%)		
occurrences (all)	7		
Peripheral swelling			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	4 / 99 (4.04%)		
occurrences (all)	4		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	3 / 99 (3.03%)		
occurrences (all)	3		
Seasonal allergy			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Vaginal inflammation			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Vulvovaginal dryness			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	99 / 99 (100.00%)		
occurrences (all)	9		
Dysphonia			
subjects affected / exposed	2 / 99 (2.02%)		
occurrences (all)	2		
Dyspnoea			
subjects affected / exposed	10 / 99 (10.10%)		
occurrences (all)	12		
Dyspnoea exertional			
subjects affected / exposed	2 / 99 (2.02%)		
occurrences (all)	2		
Epistaxis			
subjects affected / exposed	23 / 99 (23.23%)		
occurrences (all)	26		
Nasal dryness			
subjects affected / exposed	2 / 99 (2.02%)		
occurrences (all)	2		
Oropharyngeal pain			
subjects affected / exposed	3 / 99 (3.03%)		
occurrences (all)	3		
Pulmonary embolism			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Rhinorrhoea			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Initial insomnia			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Insomnia			

subjects affected / exposed	6 / 99 (6.06%)		
occurrences (all)	6		
Restlessness			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	30 / 99 (30.30%)		
occurrences (all)	36		
Aspartate aminotransferase increased			
subjects affected / exposed	38 / 99 (38.38%)		
occurrences (all)	57		
Blood bilirubin increased			
subjects affected / exposed	3 / 99 (3.03%)		
occurrences (all)	4		
Blood creatinine increased			
subjects affected / exposed	5 / 99 (5.05%)		
occurrences (all)	6		
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
C-reactive protein increased			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Cardiovascular function test abnormal			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Electrocardiogram abnormal			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Electrocardiogram T wave inversion			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Gamma-glutamyltransferase increased			

subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Haematocrit decreased			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Haemoglobin increased			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Nitrite urine			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Weight decreased			
subjects affected / exposed	2 / 99 (2.02%)		
occurrences (all)	2		
White blood cell count increased			
subjects affected / exposed	2 / 99 (2.02%)		
occurrences (all)	2		
White blood cells urine positive			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Post procedural haemorrhage			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Skin laceration			
subjects affected / exposed	2 / 99 (2.02%)		
occurrences (all)	2		
Spinal fracture			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Transfusion related complication			

subjects affected / exposed occurrences (all)	1 / 99 (1.01%) 1		
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Cardiovascular disorder			
subjects affected / exposed	3 / 99 (3.03%)		
occurrences (all)	3		
Mitral valve disease			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Palpitations			
subjects affected / exposed	5 / 99 (5.05%)		
occurrences (all)	5		
Nervous system disorders			
Dizziness			
subjects affected / exposed	5 / 99 (5.05%)		
occurrences (all)	6		
Dysgeusia			
subjects affected / exposed	12 / 99 (12.12%)		
occurrences (all)	12		
Headache			
subjects affected / exposed	12 / 99 (12.12%)		
occurrences (all)	14		
Paraesthesia			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Polyneuropathy			
subjects affected / exposed	75 / 99 (75.76%)		
occurrences (all)	102		
Sciatica			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Syncope			

subjects affected / exposed	2 / 99 (2.02%)		
occurrences (all)	2		
Vertigo			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	86 / 99 (86.87%)		
occurrences (all)	151		
Febrile neutropenia			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Leukopenia			
subjects affected / exposed	4 / 99 (4.04%)		
occurrences (all)	6		
Lymph node pain			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Lymphadenopathy			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Neutropenia			
subjects affected / exposed	56 / 99 (56.57%)		
occurrences (all)	101		
Thrombocytopenia			
subjects affected / exposed	22 / 99 (22.22%)		
occurrences (all)	30		
Thrombocytosis			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	2		
Vertigo			

subjects affected / exposed occurrences (all)	1 / 99 (1.01%) 1		
Eye disorders			
Chalazion			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Dry eye			
subjects affected / exposed	4 / 99 (4.04%)		
occurrences (all)	4		
Keratitis			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Lacrimation increased			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Visual impairment			
subjects affected / exposed	4 / 99 (4.04%)		
occurrences (all)	5		
Vitreous degeneration			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	4 / 99 (4.04%)		
occurrences (all)	4		
Abdominal pain upper			
subjects affected / exposed	9 / 99 (9.09%)		
occurrences (all)	10		
Anal fissure			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Constipation			

subjects affected / exposed	13 / 99 (13.13%)		
occurrences (all)	14		
Diarrhoea			
subjects affected / exposed	83 / 99 (83.84%)		
occurrences (all)	180		
Diverticulum			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Dry mouth			
subjects affected / exposed	12 / 99 (12.12%)		
occurrences (all)	13		
Dyspepsia			
subjects affected / exposed	15 / 99 (15.15%)		
occurrences (all)	19		
Flatulence			
subjects affected / exposed	2 / 99 (2.02%)		
occurrences (all)	2		
Gastritis			
subjects affected / exposed	2 / 99 (2.02%)		
occurrences (all)	2		
Gastrooesophageal reflux disease			
subjects affected / exposed	5 / 99 (5.05%)		
occurrences (all)	7		
Gingival bleeding			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	2		
Haematochezia			
subjects affected / exposed	2 / 99 (2.02%)		
occurrences (all)	2		
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Haemorrhoids			
subjects affected / exposed	2 / 99 (2.02%)		
occurrences (all)	2		
Lactose intolerance			

subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	47 / 99 (47.47%)		
occurrences (all)	81		
Salivary duct inflammation			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Stomatitis			
subjects affected / exposed	44 / 99 (44.44%)		
occurrences (all)	65		
Hepatobiliary disorders			
Hepatotoxicity			
subjects affected / exposed	16 / 99 (16.16%)		
occurrences (all)	21		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	16 / 99 (16.16%)		
occurrences (all)	16		
Dermatitis bullous			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Dry skin			
subjects affected / exposed	4 / 99 (4.04%)		
occurrences (all)	4		
Eczema			
subjects affected / exposed	4 / 99 (4.04%)		
occurrences (all)	4		
Erythema			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Nail bed inflammation			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Nail disorder			

subjects affected / exposed	6 / 99 (6.06%)		
occurrences (all)	6		
Nail toxicity			
subjects affected / exposed	11 / 99 (11.11%)		
occurrences (all)	11		
Onycholysis			
subjects affected / exposed	3 / 99 (3.03%)		
occurrences (all)	3		
Palmar-plantar erythrodysesthesia syndrome			
subjects affected / exposed	3 / 99 (3.03%)		
occurrences (all)	3		
Pruritus			
subjects affected / exposed	3 / 99 (3.03%)		
occurrences (all)	4		
Rash			
subjects affected / exposed	12 / 99 (12.12%)		
occurrences (all)	14		
Skin toxicity			
subjects affected / exposed	47 / 99 (47.47%)		
occurrences (all)	63		
Skin ulcer			
subjects affected / exposed	2 / 99 (2.02%)		
occurrences (all)	2		
Solar dermatitis			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Toxic epidermal necrolysis			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	12 / 99 (12.12%)		
occurrences (all)	14		
Glycosuria			

subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Haematuria			
subjects affected / exposed	3 / 99 (3.03%)		
occurrences (all)	3		
Hydronephrosis			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Leukocyturia			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Micturition urgency			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Pollakiuria			
subjects affected / exposed	2 / 99 (2.02%)		
occurrences (all)	3		
Proteinuria			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Renal paindd			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 99 (4.04%)		
occurrences (all)	5		
Back pain			
subjects affected / exposed	7 / 99 (7.07%)		
occurrences (all)	9		
Bone pain			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	2		
Flank pain			

subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Muscle spasms			
subjects affected / exposed	4 / 99 (4.04%)		
occurrences (all)	4		
Myalgia			
subjects affected / exposed	8 / 99 (8.08%)		
occurrences (all)	8		
Pain in extremity			
subjects affected / exposed	6 / 99 (6.06%)		
occurrences (all)	7		
Infections and infestations			
Bacteriuria			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Candida infection			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Cystitis			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Erysipelas			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Folliculitis			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Fungal skin infection			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Furuncle			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		

Herpes simplex			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	2		
Influenza			
subjects affected / exposed	2 / 99 (2.02%)		
occurrences (all)	2		
Nasopharyngitis			
subjects affected / exposed	10 / 99 (10.10%)		
occurrences (all)	13		
Respiratory tract infection			
subjects affected / exposed	9 / 99 (9.09%)		
occurrences (all)	10		
Sinusitis			
subjects affected / exposed	2 / 99 (2.02%)		
occurrences (all)	2		
Urinary tract infection			
subjects affected / exposed	7 / 99 (7.07%)		
occurrences (all)	9		
Vaginal infection			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Vulvovaginal candidiasis			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	7 / 99 (7.07%)		
occurrences (all)	7		
Hyperkalaemia			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Hypocalcaemia			
subjects affected / exposed	2 / 99 (2.02%)		
occurrences (all)	3		
Hypokalaemia			

subjects affected / exposed	15 / 99 (15.15%)		
occurrences (all)	21		
Hypomagnesaemia			
subjects affected / exposed	6 / 99 (6.06%)		
occurrences (all)	7		
Hyponatraemia			
subjects affected / exposed	2 / 99 (2.02%)		
occurrences (all)	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