Clinical trial results:
Randomized, Open-Label, Phase 2 Study of the Efficacy and Safety of Weekly Paclitaxel Single-Agent and Two Different Regimens of the Poly ADP Ribose Polymerase-1 Inhibitor SAR240550 (BSI-201) in Combination with Weekly Paclitaxel, as Neoadjuvant Therapy in Patients with Stage II-IIIA Triple Negative Breast Cancer (TNBC)

Summary

EudraCT number	2010-018960-17
Trial protocol	ES FR DE
Global end of trial date	28 February 2017

Results information

Result version number	v1 (current)
This version publication date	14 March 2018
First version publication date	14 March 2018

Trial information

Trial identification

Sponsor protocol code	TCD11419

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01204125
WHO universal trial number (UTN)	-
Other trial identifiers	STUDY NAME: SOLTI NeoPARP

Notes:

Sponsors

Sponsor organisation name	Sanofi aventis recherche & développement
Sponsor organisation address	1 avenue Pierre Brossolette, Chilly-Mazarin, France, 91380
Public contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 April 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 February 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to assess the pathologic complete response (pCR) rate in the breast of subjects with operable Stage II to IIIA triple-negative breast cancer (TNBC) treated with paclitaxel weekly + SAR240550 (iniparib) twice weekly (paclitaxel + tw-iniparib arm), with paclitaxel weekly + iniparib weekly (paclitaxel + w-iniparib arm), and with paclitaxel weekly as a single-agent reference treatment (paclitaxel-only arm).

Protection of trial subjects:

Subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency. Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 September 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 95
Country: Number of subjects enrolled	France: 39
Country: Number of subjects enrolled	Germany: 7
Worldwide total number of subjects	141
EEA total number of subjects	141

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)	119
From 65 to 84 years	22
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 24 centres in 3 European countries between 20 September 2010 and 28 February 2017.

Pre-assignment

Screening details:

A total of 141 subjects were enrolled and randomised in a 1:1:1 ratio to paclitaxel-only arm, paclitaxel + w (once per week)-iniparib arm, and paclitaxel + tw (twice per week)-iniparib arm according to the following stratification factors: axillary nodal involvement (yes or no) and tumor size (=<5 cm or >5 cm).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Paclitaxel

Arm description:

Paclitaxel 80 mg/m^2 intravenous (IV) infusion on Day 1 of 12 cycles of 7 days each, until disease progression (DP), unacceptable toxicity or subject's refusal (maximum duration up to 15 weeks).

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

Dosage and administration details:

Paclitaxel was administered on Day 1 of 12 cycles of 7 days each (maximum duration up to 15 weeks).

Arm title	Paclitaxel + Iniparib Once Weekly

Arm description:

Paclitaxel 80 mg/m^2 IV infusion on Day 1 of 12 cycles of 7 days each, in combination with iniparib 11.2 mg/kg IV once weekly (Day 1) for a maximum of 12 administrations, until DP, unacceptable toxicity or subject's refusal (maximum duration up to 15 weeks).

Arm type	Experimental
Investigational medicinal product name	Non IMP: Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Paclitaxel was administered on Day 1 of 12 cycles of 7 days each, up to 12 IV infusions (maximum duration up to 15 weeks).

Investigational medicinal product name	Iniparib
Investigational medicinal product code	SAR2405550
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Iniparib infusion started within 1 hour after the end of paclitaxel administration on Day 1 of each week in the paclitaxel + w-iniparib arm over a total period up to 15 weeks.

Arm title	Paclitaxel + Iniparib Twice Weekly

Arm description:

Paclitaxel 80 mg/m^2 IV infusion on Day 1 of 12 cycles of 7 days each, in combination with iniparib 5.6 mg/kg IV twice weekly (Day 1 and Day 4) for a maximum of 24 administrations, until DP, unacceptable toxicity or subject's refusal (maximum duration up to 15 weeks).

Arm type	Experimental
Investigational medicinal product name	Non IMP: Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Paclitaxel was administered on Day 1 of 12 cycles of 7 days each, up to 12 IV infusions (maximum duration up to 15 weeks).

Investigational medicinal product name	Iniparib
Investigational medicinal product code	SAR2405550
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Iniparib infusion started within 1 hour after the end of paclitaxel administration on Day 1 and Day 4 of each week in the paclitaxel + tw- iniparib arm over a total period up to 15 weeks.

Number of subjects in period 1	Paclitaxel	Paclitaxel + Iniparib Once Weekly	Paclitaxel + Iniparib Twice Weekly
Started	47	46	48
Completed	39	38	39
Not completed	8	8	9
Other than specified above	4	2	1
Randomized not treated	1	-	-
Adverse Event	1	2	1
Disease Progression	2	4	7

Baseline characteristics

Reporting groups	
Reporting group title	Paclitaxel
Reporting group description:	
Paclitaxel 80 mg/m^2 intravenous (IV) infusion on Day 1 of 12 cycles of 7 days each, until disease progression (DP), unacceptable toxicity or subject's refusal (maximum duration up to 15 weeks).	
Reporting group title	Paclitaxel + Iniparib Once Weekly
Reporting group description:	
Paclitaxel 80 mg/m^2 IV infusion on Day 1 of 12 cycles of 7 days each, in combination with iniparib 11.2 mg/kg IV once weekly (Day 1) for a maximum of 12 administrations, until DP, unacceptable toxicity or subject's refusal (maximum duration up to 15 weeks).	
Reporting group title	Paclitaxel + Iniparib Twice Weekly
Reporting group description:	
Paclitaxel 80 mg/m^2 IV infusion on Day 1 of 12 cycles of 7 days each, in combination with iniparib 5.6 mg/kg IV twice weekly (Day 1 and Day 4) for a maximum of 24 administrations, until DP, unacceptable toxicity or subject's refusal (maximum duration up to 15 weeks).	

Reporting group values	Paclitaxel	Paclitaxel + Iniparib Once Weekly	Paclitaxel + Iniparib Twice Weekly
Number of subjects	47	46	48
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	52.9	50.9	50.1
standard deviation	± 10.3	± 14.3	± 12.2
Gender categorical			
Units: Subjects			
Female	47	46	48
Male	0	0	0

Reporting group values	Total		
Number of subjects	141		
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	141		
Male	0		

End points

End points reporting groups

Reporting group title	Paclitaxel

Reporting group description:

Paclitaxel 80 mg/m^2 intravenous (IV) infusion on Day 1 of 12 cycles of 7 days each, until disease progression (DP), unacceptable toxicity or subject's refusal (maximum duration up to 15 weeks).

Reporting group title	Paclitaxel + Iniparib Once Weekly

Reporting group description:

Paclitaxel 80 mg/m^2 IV infusion on Day 1 of 12 cycles of 7 days each, in combination with iniparib 11.2 mg/kg IV once weekly (Day 1) for a maximum of 12 administrations, until DP, unacceptable toxicity or subject's refusal (maximum duration up to 15 weeks).

Reporting group title	Paclitaxel + Iniparib Twice Weekly

Reporting group description:

Paclitaxel 80 mg/m^2 IV infusion on Day 1 of 12 cycles of 7 days each, in combination with iniparib 5.6 mg/kg IV twice weekly (Day 1 and Day 4) for a maximum of 24 administrations, until DP, unacceptable toxicity or subject's refusal (maximum duration up to 15 weeks).

Primary: Percentage of Subjects With Pathological Complete Response (PCR) Rate in Breast

End point title	Percentage of Subjects With Pathological Complete Response (PCR) Rate in Breast[1]

End point description:

PCR rate in breast was defined as the complete absence of invasive carcinoma on histological examination of the breast at the time of definitive surgery and confirmed by a centralized, blinded review. Analysis was performed on Intent-to-treat (ITT) population that included all randomized subjects who had given their informed consent and for whom there was confirmation of successful allocation of a randomization number through the interactive voice response system (IVRS).

End point type	Primary

End point timeframe:

Baseline up to the 4 weeks after last dose of study drug on Week 15 (up to Week 19)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Paclitaxel	Paclitaxel + Iniparib Once Weekly	Paclitaxel + Iniparib Twice Weekly	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	47	46	48	
Units: Percentage of subjects				
number (confidence interval 95%)	21.3 (10.7 to 35.7)	21.7 (10.9 to 36.4)	18.8 (8.9 to 32.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With PCR Rate in Breast and Axilla

End point title	Percentage of Subjects With PCR Rate in Breast and Axilla

End point description:

PCR rate in the breast and axilla was defined as the complete absence of invasive carcinoma on histological examination at the time of definitive surgery as assessed and confirmed by centralized, blinded review. Analysis was performed on ITT population.

End point type	Secondary

End point timeframe:

Baseline up to the 4 weeks after last dose of study drug on Week 15 (up to Week 19)

End point values	Paclitaxel	Paclitaxel + Iniparib Once Weekly	Paclitaxel + Iniparib Twice Weekly	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	47	46	48	
Units: Percentage of subjects				
number (confidence interval 95%)	21.3 (10.7 to 35.7)	17.4 (7.8 to 31.4)	18.8 (8.9 to 32.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Best Overall Response

End point title	Percentage of Subjects With Best Overall Response

End point description:

Best overall response was defined as best response (in order of confirmed complete response [CR], confirmed partial response [PR], stable disease [SD] & progressive disease [PD]) among all overall response based on RECIST 1.1. CR was defined as disappearance of all target/non-target lesions and normalization of tumor marker level. Any pathological lymph nodes (target/non-target) must have reduction in short axis to <10 mm. PR was defined as at least a 30% decrease in sum of diameters of target lesions, taking as reference to baseline sum diameters. Stable Disease (SD): Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference to smallest sum diameter since the treatment started and Progressive Disease (PD): At least a 20% increase in the sum diameter of target lesions, taking as reference the smallest sum LD recorded since the treatment started or the appearance of one or more new lesions. Analysis was performed on ITT population.

End point type	Secondary

End point timeframe:

Baseline up to tumor progression or death due to any cause or study cut-off date, whichever occurs first (maximum duration: 1.5 years)

End point values	Paclitaxel	Paclitaxel + Iniparib Once Weekly	Paclitaxel + Iniparib Twice Weekly	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	47	46	48	
Units: Percentage of subjects				
number (not applicable)				

Complete response	6.4	0	4.2	
Partial response	53.2	60.9	58.3	
Stable disease	31.9	32.6	25.0	
Progressive disease	4.3	4.3	12.5	
Not evaluable	4.3	2.2	0	
Overall response rate (CR+PR)	59.6	60.9	62.5	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Breast Conservation

End point title	Percentage of Subjects With Breast Conservation

End point description:

Breast conservation rate (BCR) was defined as the proportion of subjects with limited breast surgery after the study treatment. Analysis was performed on ITT population.

End point type	Secondary

End point timeframe:

Baseline up to tumor progression or death due to any cause or study cut-off date, whichever occurs first (maximum duration: 1.5 years)

End point values	Paclitaxel	Paclitaxel + Iniparib Once Weekly	Paclitaxel + Iniparib Twice Weekly	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	47	46	48	
Units: Percentage of subjects				
number (confidence interval 95%)	53.2 (38.1 to 67.9)	54.3 (39.0 to 69.1)	50.0 (35.2 to 64.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Treatment Emergent Adverse Event (TEAE)

End point title	Percentage of Subjects With Treatment Emergent Adverse Event (TEAE)

End point description:

Any untoward medical occurrence in a subject who received investigational medicinal product (IMP) was considered an AE without regard to possibility of causal relationship with this treatment. TEAEs were defined as AEs that developed or worsened or became serious during on-treatment period. On-treatment period was defined as the time from the IMP until 30 days after the last administration of IMP. A serious adverse event (SAE) was defined as any untoward medical occurrence that resulted in any of the following outcomes: death, life-threatening, required initial or prolonged in-subject hospitalization, persistent or significant disability/incapacity, congenital anomaly/birth defect, or considered as medically important event. Any TEAE included subjects with both serious and non-serious AEs. Analysis was performed on safety population which was defined as subset of randomized subjects who received at least 1 (even incomplete) part of the study treatments.

End point type	Secondary

End point timeframe:

Baseline up to 30 days after last dose of study drug (maximum duration: 1.5 years)

End point values	Paclitaxel	Paclitaxel + Iniparib Once Weekly	Paclitaxel + Iniparib Twice Weekly	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	47	46	48	
Units: Percentage of subjects				
number (not applicable)				
Any TEAE	93.5	97.8	97.9	
Any treatment-emergent SAE	4.3	4.3	4.2	
Any TEAE leading to permanent discontinuation	2.2	4.3	2.1	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Disease free survival (DFS)

End point title	Percentage of Subjects With Disease free survival (DFS)

End point description:

DFS was defined as the interval from the date of randomization to the date of local, regional or metastatic relapse or the date of second primary cancer or death from any cause whichever occurs first. Data for this end point was not analysed based on sponsor's discretion.

End point type	Secondary

End point timeframe:

Baseline up to tumor progression or death due to any cause or end of follow up period, whichever occurs first (maximum duration: 6.6 years)

End point values	Paclitaxel	Paclitaxel + Iniparib Once Weekly	Paclitaxel + Iniparib Twice Weekly	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[2]	0[3]	0[4]	
Units: percentage of subjects				
number (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[2] - Due to change in planned analysis, based on sponsor's discretion, data for this was not analyzed.

[3] - Due to change in planned analysis, based on sponsor's discretion, data for this was not analyzed.

[4] - Due to change in planned analysis, based on sponsor's discretion, data for this was not analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Overall Survival

End point title	Percentage of Subjects With Overall Survival

End point description:

Overall survival was defined as the time interval from the date of randomization to the date of death due to any cause. Data for this end point was not analysed based on sponsor's discretion.

End point type	Secondary

End point timeframe:

Baseline up to tumor progression or death due to any cause or end of follow up period, whichever occurs first (maximum duration: 6.6 years)

End point values	Paclitaxel	Paclitaxel + Iniparib Once Weekly	Paclitaxel + Iniparib Twice Weekly	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[5]	0[6]	0[7]	
Units: percentage of subjects				
number (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[5] - Due to change in planned analysis, based on sponsor's discretion, data for this was not analyzed.

[6] - Due to change in planned analysis, based on sponsor's discretion, data for this was not analyzed.

[7] - Due to change in planned analysis, based on sponsor's discretion, data for this was not analyzed.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All Adverse Events (AEs) were collected from signature of the informed consent form up to the final visit (maximum duration: 6.6 years) regardless of seriousness or relationship to investigational product.

Adverse event reporting additional description:

Reported AEs are TEAEs that is AEs that developed/worsened during the 'on treatment period' (from first study treatment administration until 30 days after the last administration of study treatment). Analysis was performed on safety population.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Paclitaxel

Reporting group description:

Paclitaxel 80 mg/m^2 IV infusion on Day 1 of 12 cycles of 7 days each, until DP, unacceptable toxicity or subject's refusal (maximum duration up to 15 weeks).

Reporting group title	Paclitaxel + Iniparib Once Weekly

Reporting group description:

Paclitaxel 80 mg/m^2 IV infusion on Day 1 of 12 cycles of 7 days each, in combination with iniparib 11.2 mg/kg IV once weekly (Day 1) for a maximum of 12 administrations, until DP, unacceptable toxicity or subject's refusal (maximum duration up to 15 weeks).

Reporting group title	Paclitaxel + Iniparib Twice Weekly

Reporting group description:

Paclitaxel 80 mg/m^2 IV infusion on Day 1 of 12 cycles of 7 days each, in combination with iniparib 5.6 mg/kg IV twice weekly (Day 1 and Day 4) for a maximum of 24 administrations, until DP, unacceptable toxicity or subject's refusal (maximum duration up to 15 weeks).

Serious adverse events	Paclitaxel	Paclitaxel + Iniparib Once Weekly	Paclitaxel + Iniparib Twice Weekly
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 46 (6.52%)	2 / 46 (4.35%)	2 / 48 (4.17%)
number of deaths (all causes)	3	15	12
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Radius Fracture			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion Spontaneous			

subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary Embolism			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Atypical Pneumonia			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected Skin Ulcer			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Paclitaxel	Paclitaxel + Iniparib Once Weekly	Paclitaxel + Iniparib Twice Weekly
Total subjects affected by non-serious adverse events			
subjects affected / exposed	43 / 46 (93.48%)	45 / 46 (97.83%)	47 / 48 (97.92%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour Pain			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	1 / 48 (2.08%)
occurrences (all)	0	2	1
Vascular disorders			

Flushing			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	2 / 48 (4.17%)
occurrences (all)	0	1	2
Haematoma			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	1 / 48 (2.08%)
occurrences (all)	0	1	1
Hot Flush			
subjects affected / exposed	5 / 46 (10.87%)	3 / 46 (6.52%)	5 / 48 (10.42%)
occurrences (all)	5	3	5
Hypertension			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	2 / 48 (4.17%)
occurrences (all)	0	1	2
Lymphocele			
subjects affected / exposed	1 / 46 (2.17%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences (all)	1	1	0
Lymphoedema			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Phlebitis			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Vascular Pain			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
Vein Disorder			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences (all)	0	2	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	26 / 46 (56.52%)	21 / 46 (45.65%)	24 / 48 (50.00%)
occurrences (all)	38	30	41
Axillary Pain			
subjects affected / exposed	0 / 46 (0.00%)	3 / 46 (6.52%)	0 / 48 (0.00%)
occurrences (all)	0	3	0
Catheter Site Pain			

subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Catheter Site Related Reaction			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
Chest Discomfort			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Chest Pain			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Chills			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Face Oedema			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	1	0	1
Fatigue			
subjects affected / exposed	8 / 46 (17.39%)	6 / 46 (13.04%)	6 / 48 (12.50%)
occurrences (all)	11	8	8
Influenza Like Illness			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	2 / 48 (4.17%)
occurrences (all)	0	0	2
Infusion Site Extravasation			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
Infusion Site Pain			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	2 / 48 (4.17%)
occurrences (all)	0	1	2
Injection Site Pain			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Mucosal Dryness			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
Non-Cardiac Chest Pain			

subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
Oedema			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
Oedema Peripheral			
subjects affected / exposed	4 / 46 (8.70%)	1 / 46 (2.17%)	5 / 48 (10.42%)
occurrences (all)	4	1	6
Pain			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Puncture Site Pain			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	2 / 46 (4.35%)	4 / 46 (8.70%)	0 / 48 (0.00%)
occurrences (all)	2	5	0
Immune system disorders			
Drug Hypersensitivity			
subjects affected / exposed	1 / 46 (2.17%)	2 / 46 (4.35%)	4 / 48 (8.33%)
occurrences (all)	1	2	4
Hypersensitivity			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	2	0	1
Reproductive system and breast disorders			
Adnexa Uteri Pain			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Amenorrhoea			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Breast Discomfort			
subjects affected / exposed	1 / 46 (2.17%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences (all)	1	1	0
Breast Oedema			

subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
Breast Pain			
subjects affected / exposed	0 / 46 (0.00%)	2 / 46 (4.35%)	2 / 48 (4.17%)
occurrences (all)	0	3	2
Dysmenorrhoea			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	1 / 48 (2.08%)
occurrences (all)	0	1	1
Genital Tract Inflammation			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
Menstruation Irregular			
subjects affected / exposed	1 / 46 (2.17%)	1 / 46 (2.17%)	3 / 48 (6.25%)
occurrences (all)	1	1	3
Nipple Exudate Bloody			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Pelvic Pain			
subjects affected / exposed	2 / 46 (4.35%)	1 / 46 (2.17%)	1 / 48 (2.08%)
occurrences (all)	2	1	1
Vaginal Haemorrhage			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	1 / 48 (2.08%)
occurrences (all)	0	1	1
Respiratory, thoracic and mediastinal disorders			
Catarrh			
subjects affected / exposed	2 / 46 (4.35%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	2	0	2
Cough			
subjects affected / exposed	3 / 46 (6.52%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	3	0	1
Dysphonia			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Dyspnoea			

subjects affected / exposed	1 / 46 (2.17%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences (all)	1	1	0
Epistaxis			
subjects affected / exposed	6 / 46 (13.04%)	3 / 46 (6.52%)	4 / 48 (8.33%)
occurrences (all)	7	5	4
Nasal Dryness			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Nasal Inflammation			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal Pain			
subjects affected / exposed	1 / 46 (2.17%)	1 / 46 (2.17%)	1 / 48 (2.08%)
occurrences (all)	1	1	1
Rhinorrhoea			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Anhedonia			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
Anxiety			
subjects affected / exposed	0 / 46 (0.00%)	2 / 46 (4.35%)	4 / 48 (8.33%)
occurrences (all)	0	2	4
Depression			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	1 / 46 (2.17%)	5 / 46 (10.87%)	3 / 48 (6.25%)
occurrences (all)	1	6	3
Investigations			
Alanine Aminotransferase Increased			

subjects affected / exposed	1 / 46 (2.17%)	1 / 46 (2.17%)	1 / 48 (2.08%)
occurrences (all)	1	1	1
Blood Calcium Decreased			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Blood Glucose Increased			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	1 / 48 (2.08%)
occurrences (all)	0	1	1
Blood Potassium Decreased			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Haemoglobin Decreased			
subjects affected / exposed	1 / 46 (2.17%)	1 / 46 (2.17%)	1 / 48 (2.08%)
occurrences (all)	1	1	1
Weight Increased			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	2 / 48 (4.17%)
occurrences (all)	1	0	2
Injury, poisoning and procedural complications			
Arthropod Bite			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
Arthropod Sting			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Infusion Related Reaction			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	3 / 48 (6.25%)
occurrences (all)	0	0	12
Ligament Sprain			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
Procedural Pain			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
Rib Fracture			

subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Seroma			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	2 / 46 (4.35%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences (all)	2	1	0
Tachycardia			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Aphonia			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	1 / 46 (2.17%)	4 / 46 (8.70%)	3 / 48 (6.25%)
occurrences (all)	1	4	3
Dysgeusia			
subjects affected / exposed	5 / 46 (10.87%)	4 / 46 (8.70%)	6 / 48 (12.50%)
occurrences (all)	7	4	11
Headache			
subjects affected / exposed	6 / 46 (13.04%)	8 / 46 (17.39%)	10 / 48 (20.83%)
occurrences (all)	7	9	10
Hypoaesthesia			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	2 / 48 (4.17%)
occurrences (all)	0	0	2
Migraine			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	1 / 48 (2.08%)
occurrences (all)	0	1	1
Neuropathy Peripheral			

subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	1 / 48 (2.08%)
occurrences (all)	0	2	1
Neurotoxicity			
subjects affected / exposed	4 / 46 (8.70%)	4 / 46 (8.70%)	2 / 48 (4.17%)
occurrences (all)	5	4	3
Paraesthesia			
subjects affected / exposed	8 / 46 (17.39%)	5 / 46 (10.87%)	4 / 48 (8.33%)
occurrences (all)	8	7	4
Peripheral Sensory Neuropathy			
subjects affected / exposed	13 / 46 (28.26%)	10 / 46 (21.74%)	14 / 48 (29.17%)
occurrences (all)	14	12	17
Presyncope			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Somnolence			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
Syncope			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 46 (2.17%)	1 / 46 (2.17%)	3 / 48 (6.25%)
occurrences (all)	2	1	4
Leukopenia			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Lymphopenia			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	2 / 48 (4.17%)
occurrences (all)	0	1	2
Neutropenia			
subjects affected / exposed	2 / 46 (4.35%)	3 / 46 (6.52%)	5 / 48 (10.42%)
occurrences (all)	4	4	5
Ear and labyrinth disorders			
Ear Pain			

subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
External Ear Inflammation			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Hypoacusis			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Vertigo			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	5 / 48 (10.42%)
occurrences (all)	1	0	6
Eye disorders			
Dry Eye			
subjects affected / exposed	3 / 46 (6.52%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences (all)	3	1	0
Eye Irritation			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	1 / 48 (2.08%)
occurrences (all)	0	1	1
Eye Pruritus			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
Eyelid Oedema			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Lacrimation Increased			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	1	0	1
Vision Blurred			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Visual Acuity Reduced			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal Discomfort			

subjects affected / exposed	1 / 46 (2.17%)	1 / 46 (2.17%)	1 / 48 (2.08%)
occurrences (all)	1	1	1
Abdominal Distension			
subjects affected / exposed	1 / 46 (2.17%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences (all)	1	1	0
Abdominal Pain			
subjects affected / exposed	4 / 46 (8.70%)	4 / 46 (8.70%)	2 / 48 (4.17%)
occurrences (all)	4	6	2
Abdominal Pain Upper			
subjects affected / exposed	3 / 46 (6.52%)	2 / 46 (4.35%)	1 / 48 (2.08%)
occurrences (all)	3	2	1
Anal Fissure			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	5 / 46 (10.87%)	7 / 46 (15.22%)	5 / 48 (10.42%)
occurrences (all)	6	8	7
Diarrhoea			
subjects affected / exposed	7 / 46 (15.22%)	18 / 46 (39.13%)	14 / 48 (29.17%)
occurrences (all)	7	23	23
Dry Mouth			
subjects affected / exposed	1 / 46 (2.17%)	1 / 46 (2.17%)	2 / 48 (4.17%)
occurrences (all)	1	1	2
Dyspepsia			
subjects affected / exposed	3 / 46 (6.52%)	3 / 46 (6.52%)	3 / 48 (6.25%)
occurrences (all)	3	4	3
Flatulence			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	1	0	1
Gastritis			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal Pain			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	2 / 48 (4.17%)
occurrences (all)	1	0	2
Gastrooesophageal Reflux Disease			

subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Haematochezia			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	1 / 48 (2.08%)
occurrences (all)	0	1	1
Haemorrhoids			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	1	0	1
Nausea			
subjects affected / exposed	4 / 46 (8.70%)	7 / 46 (15.22%)	11 / 48 (22.92%)
occurrences (all)	5	11	15
Obstruction Gastric			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Odynophagia			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Rectal Haemorrhage			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
Stomatitis			
subjects affected / exposed	4 / 46 (8.70%)	6 / 46 (13.04%)	8 / 48 (16.67%)
occurrences (all)	4	7	12
Vomiting			
subjects affected / exposed	3 / 46 (6.52%)	2 / 46 (4.35%)	5 / 48 (10.42%)
occurrences (all)	4	2	9
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 46 (2.17%)	1 / 46 (2.17%)	3 / 48 (6.25%)
occurrences (all)	1	1	3
Alopecia			
subjects affected / exposed	34 / 46 (73.91%)	28 / 46 (60.87%)	33 / 48 (68.75%)
occurrences (all)	35	28	33
Blister			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1

Dermatitis			
subjects affected / exposed	1 / 46 (2.17%)	1 / 46 (2.17%)	1 / 48 (2.08%)
occurrences (all)	1	1	1
Dermatitis Acneiform			
subjects affected / exposed	1 / 46 (2.17%)	3 / 46 (6.52%)	1 / 48 (2.08%)
occurrences (all)	1	4	1
Dermatitis Allergic			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	1 / 48 (2.08%)
occurrences (all)	0	1	2
Dry Skin			
subjects affected / exposed	3 / 46 (6.52%)	1 / 46 (2.17%)	1 / 48 (2.08%)
occurrences (all)	3	1	1
Eczema			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	2 / 46 (4.35%)	3 / 46 (6.52%)	5 / 48 (10.42%)
occurrences (all)	2	5	6
Generalised Erythema			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
Nail Disorder			
subjects affected / exposed	6 / 46 (13.04%)	3 / 46 (6.52%)	2 / 48 (4.17%)
occurrences (all)	6	3	2
Nail Ridging			
subjects affected / exposed	1 / 46 (2.17%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences (all)	1	1	0
Nail Toxicity			
subjects affected / exposed	2 / 46 (4.35%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences (all)	2	1	0
Onychalgia			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Onycholysis			
subjects affected / exposed	0 / 46 (0.00%)	2 / 46 (4.35%)	0 / 48 (0.00%)
occurrences (all)	0	2	0

Onychomadesis			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Palmar-Plantar Erythrodysaesthesia Syndrome			
subjects affected / exposed	0 / 46 (0.00%)	3 / 46 (6.52%)	1 / 48 (2.08%)
occurrences (all)	0	3	1
Pruritus			
subjects affected / exposed	2 / 46 (4.35%)	4 / 46 (8.70%)	2 / 48 (4.17%)
occurrences (all)	2	7	2
Rash			
subjects affected / exposed	7 / 46 (15.22%)	3 / 46 (6.52%)	6 / 48 (12.50%)
occurrences (all)	10	3	7
Rash Erythematous			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Rash Maculo-Papular			
subjects affected / exposed	1 / 46 (2.17%)	1 / 46 (2.17%)	1 / 48 (2.08%)
occurrences (all)	1	1	1
Rash Pruritic			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Scab			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Skin Fissures			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
Skin Hyperpigmentation			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Skin Lesion			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	1	0	1
Skin Ulcer			

subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Solar Lentigo			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Swelling Face			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
Urticaria			
subjects affected / exposed	2 / 46 (4.35%)	2 / 46 (4.35%)	0 / 48 (0.00%)
occurrences (all)	3	2	0
Xeroderma			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	1	0	1
Renal Colic			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 46 (13.04%)	5 / 46 (10.87%)	1 / 48 (2.08%)
occurrences (all)	6	5	1
Back Pain			
subjects affected / exposed	1 / 46 (2.17%)	3 / 46 (6.52%)	1 / 48 (2.08%)
occurrences (all)	1	4	1
Bone Pain			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	3 / 48 (6.25%)
occurrences (all)	0	1	3
Muscle Contracture			

subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Muscle Spasms			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	1 / 48 (2.08%)
occurrences (all)	0	1	1
Musculoskeletal Chest Pain			
subjects affected / exposed	0 / 46 (0.00%)	2 / 46 (4.35%)	0 / 48 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal Pain			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	2 / 48 (4.17%)
occurrences (all)	1	0	3
Myalgia			
subjects affected / exposed	6 / 46 (13.04%)	5 / 46 (10.87%)	3 / 48 (6.25%)
occurrences (all)	7	5	4
Neck Pain			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Pain In Extremity			
subjects affected / exposed	2 / 46 (4.35%)	1 / 46 (2.17%)	1 / 48 (2.08%)
occurrences (all)	2	1	1
Pain In Jaw			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 46 (0.00%)	2 / 46 (4.35%)	0 / 48 (0.00%)
occurrences (all)	0	2	0
Conjunctivitis			
subjects affected / exposed	3 / 46 (6.52%)	2 / 46 (4.35%)	5 / 48 (10.42%)
occurrences (all)	3	2	6
Cystitis			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Erysipelas			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1

Folliculitis			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	2 / 48 (4.17%)
occurrences (all)	0	0	2
Gastroenteritis			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis Viral			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Herpes Virus Infection			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Herpes Zoster			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Infected Bite			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	1 / 46 (2.17%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences (all)	1	1	0
Nasopharyngitis			
subjects affected / exposed	6 / 46 (13.04%)	7 / 46 (15.22%)	5 / 48 (10.42%)
occurrences (all)	6	8	5
Neutropenic Infection			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Paronychia			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
Skin Infection			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1

Upper Respiratory Tract Infection			
subjects affected / exposed	2 / 46 (4.35%)	1 / 46 (2.17%)	0 / 48 (0.00%)
occurrences (all)	2	1	0
Urinary Tract Infection			
subjects affected / exposed	2 / 46 (4.35%)	2 / 46 (4.35%)	2 / 48 (4.17%)
occurrences (all)	3	2	3
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	1 / 46 (2.17%)	2 / 46 (4.35%)	4 / 48 (8.33%)
occurrences (all)	1	2	6
Hypercholesterolaemia			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Hyperkalaemia			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	1 / 48 (2.08%)
occurrences (all)	0	1	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 August 2010	Following amendments were made: 1-The follow-up after adjuvant breast cancer treatment was increased to 5 years. The schedule and frequency of tumor assessments were changed accordingly. After definitive surgery, subject tumor status and clinical laboratory tests are to be assessed every 3 months during the first 3 years and then every 6 months until the study cut-off date at 5 years from the date of surgery. 2-A safety assessment in the first 6 subjects receiving treatment in each experimental arm was added. Dose-limiting toxicity (DLT) definitions were provided. 3-The dose-modification section was amended to provide more detail.
17 December 2012	Following amendments were made: 1-Change to the subject follow up: Subjects were to be followed by the site accordingly to local standard of care (accordingly American Association of Medical Oncology physical examinations should be performed every 3 to 6 months for the first 3 years, every 6 to 12 months for years 4 and 5, and annually thereafter). The maximum follow up for each individual subject was until death or 5 years after definitive surgery date, whatever happened first. 2-Changes referred to the mechanism of action of SAR240550 (iniparib, BSI-201): Mechanism of action was updated as: Iniparib is a benzamide (4-iodo-3-nitrobenzamide) which is structurally related to nicotinamide. Benzamides have been shown to inhibit PARP1 activity. Iniparib binds to PARP1 in the NAD binding pocket as observed by X-ray crystallography. Iniparib inhibits PARP enzyme activity at high micromolar concentrations. However, recent pre-clinical and clinical data have indicated that iniparib does not possess characteristics typical of the PARP inhibitor class. The following observations regarding the cellular effects of iniparib have been made: 1. Iniparib induces gamma- H2AX (a marker of DNA damage) in tumor cell lines; 2. It induces cell cycle arrest in the G2/M phase in tumor cell lines; and 3. It potentiates the cell cycle effects of DNA damaging modalities in tumor cell lines. Additional targets of iniparib and its metabolites are under investigation. 3-Changes referred to the utilization of tumor biopsies for pharmacogenomic studies: Tumor tissue samples collected for pharmacogenomic purposes were to be transferred under conditions established in the protocol and informed consent from the sponsor to SOLTI group to identify molecular factors of response/resistance to paclitaxel. 4-Changes to the collection of Peripheral Blood Mononuclear Cell (PBMC) collection: Molecular characteristics assessment of the PBMC was removed from second endpoints.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to discontinuation of program, and as per sponsor's discretion, efficacy endpoints Disease-Free Survival and Overall Survival were not evaluated.

Notes: