



Clinical trial results:

A Phase 2, Multi-Center, Double-Blind, Placebo Controlled, Randomized Study of Ombrabulin in Patients with Platinum-Sensitive Recurrent Ovarian Cancer Treated With Carboplatin/Paclitaxel

Summary

EudraCT number	2010-024631-16
Trial protocol	BE DE CZ PL IT
Global end of trial date	09 July 2014

Results information

Result version number	v1 (current)
This version publication date	23 May 2016
First version publication date	23 July 2015

Trial information

Trial identification

Sponsor protocol code	EFC10260
-----------------------	----------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01332656
WHO universal trial number (UTN)	U1111-1118-5437

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-aventis.com
Scientific contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@Sanofi-aventis.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 July 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 July 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To demonstrate an improvement in Progression-Free Survival (PFS) for ombrabulin versus placebo in subjects with platinum-sensitive recurrent ovarian cancer (OC) treated with paclitaxel and carboplatin.

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:

Paclitaxel plus carboplatin were used as background chemotherapy.

Actual start date of recruitment	13 May 2011
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	Poland: 15
Country: Number of subjects enrolled	Spain: 8
Country: Number of subjects enrolled	Belgium: 15
Country: Number of subjects enrolled	Czech Republic: 19
Country: Number of subjects enrolled	France: 22
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Italy: 17
Country: Number of subjects enrolled	Russian Federation: 21
Country: Number of subjects enrolled	Ukraine: 30
Country: Number of subjects enrolled	United States: 5
Worldwide total number of subjects	154
EEA total number of subjects	98

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)	121
From 65 to 84 years	33
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 38 centers in 10 countries. A total of 154 subjects were screened between 13 May 2011 and 22 August 2012.

Pre-assignment

Screening details:

Of 154 screened subjects, 153 subjects were treated.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Placebo matched to ombrabulin on Day 1 and paclitaxel plus carboplatin (background therapy) on Day 2 of each 21-day cycle until disease progression, unacceptable toxicity or consent withdrawal.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Placebo administered over 30 minutes IV infusion.

Arm title	Ombrabulin
------------------	------------

Arm description:

Ombrabulin on Day 1 and paclitaxel plus carboplatin (background therapy) on Day 2 of each 21-day cycle until disease progression, unacceptable toxicity or consent withdrawal.

Arm type	Experimental
Investigational medicinal product name	Ombrabulin hydrochloride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ombrabulin 35 milligram per square meter (mg/m²) administered over 30 minutes IV infusion.

Number of subjects in period 1	Placebo	Ombrabulin
Started	77	77
Treated	76	77
Completed	0	0
Not completed	77	77
Other than specified here	45	47
Disease progression	10	15
Randomized but not treated	1	-
Adverse event	16	15
Poor compliance to protocol	1	-
Subject's request	4	-

Baseline characteristics

Reporting groups

Reporting group title	Placebo
-----------------------	---------

Reporting group description:

Placebo matched to ombrabulin on Day 1 and paclitaxel plus carboplatin (background therapy) on Day 2 of each 21-day cycle until disease progression, unacceptable toxicity or consent withdrawal.

Reporting group title	Ombrabulin
-----------------------	------------

Reporting group description:

Ombrabulin on Day 1 and paclitaxel plus carboplatin (background therapy) on Day 2 of each 21-day cycle until disease progression, unacceptable toxicity or consent withdrawal.

Reporting group values	Placebo	Ombrabulin	Total
Number of subjects	77	77	154
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	56.6 ± 10.2	55.9 ± 8.8	-
Gender categorical Units: Subjects			
Female	77	77	154
Male	0	0	0

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Placebo matched to ombrabulin on Day 1 and paclitaxel plus carboplatin (background therapy) on Day 2 of each 21-day cycle until disease progression, unacceptable toxicity or consent withdrawal.	
Reporting group title	Ombrabulin
Reporting group description:	
Ombrabulin on Day 1 and paclitaxel plus carboplatin (background therapy) on Day 2 of each 21-day cycle until disease progression, unacceptable toxicity or consent withdrawal.	

Primary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)
End point description:	
PFS was defined as the time interval from the date of randomization to the date of the first documented event defining disease progression or death due to any cause. Disease progression was defined as occurrence of: Radiological tumor progression assessed on CT scan and/or MRI following Response Evaluation Criteria in Solid Tumors (RECIST) (version 1.1) or a global deterioration of health status defined as symptomatic deterioration requiring treatment with an anticancer agent based on Investigator's decision. Analysis was performed on intent-to-treat (ITT) population defined as all randomized population analyzed according to the treatment arm allocated by randomization.	
End point type	Primary
End point timeframe:	
Randomization to Month 15 (max follow up time until cut-off date was 14.3 months)	

End point values	Placebo	Ombrabulin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	77		
Units: months				
median (confidence interval 95%)	10.41 (8.246 to 10.612)	8.84 (7.918 to 10.218)		

Statistical analyses

Statistical analysis title	Ombrabulin v Placebo
Comparison groups	Ombrabulin v Placebo
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8477
Method	Log-Rank test one-sided
Parameter estimate	Stratified hazard ratio
Point estimate	1.317

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.777
upper limit	2.231

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)
End point description:	
OS was defined as the time interval from the date of randomization to the date of death due to any cause. Analysis was performed on ITT population.	
End point type	Secondary
End point timeframe:	
Randomization to Month 18 (max follow up time until cut-off date was 17.3 months)	

End point values	Placebo	Ombrabulin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[1]	0 ^[2]		
Units: months				
median (confidence interval 95%)	(to)	(to)		

Notes:

[1] - Median OS was not calculated based on the small number of death events.

[2] - Median OS was not calculated based on the small number of death events.

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)
End point description:	
ORR was defined as the proportion of subjects with complete response (CR) or partial response (PR), defined by RECIST (version 1.1) criteria, regardless of confirmation. CR was defined as disappearance of all target/non-target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 millimeter. PR was defined as at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. Percentage of subjects with overall objective tumor response is reported. Analysis was performed on modified intent-to-treat population defined as subjects included in ITT population with measurable disease at baseline and who had at least 1 valid postbaseline tumor assessment.	
End point type	Secondary
End point timeframe:	
Randomization to Month 13 (max follow up time until cut-off date was 12.4 months)	

End point values	Placebo	Ombrabulin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	71		
Units: percentage of subjects				
number (confidence interval 95%)	75 (63.7 to 84.2)	74.6 (62.9 to 84.2)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All Adverse Events (AE) were collected from signature of the informed consent form up to Month 30 (the max follow-up was 29.2 months) regardless of seriousness or relationship to investigational product.

Adverse event reporting additional description:

Reported adverse events are treatment-emergent adverse events that is AEs that are reported during the 'on treatment period' (from first study treatment intake to 30 days after the last study treatment intake). Safety population: All randomized and treated subjects analyzed according to the treatment actually received.

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Placebo
-----------------------	---------

Reporting group description:

Placebo matched to ombrabulin on Day 1 and paclitaxel plus carboplatin (background therapy) on Day 2 of each 21-day cycle until disease progression, unacceptable toxicity or consent withdrawal.

Reporting group title	Ombrabulin
-----------------------	------------

Reporting group description:

Ombrabulin on Day 1 and paclitaxel plus carboplatin (background therapy) on Day 2 of each 21-day cycle until disease progression, unacceptable toxicity or consent withdrawal.

Serious adverse events	Placebo	Ombrabulin	
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 76 (18.42%)	20 / 77 (25.97%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
General disorders and administration site conditions			
Device Occlusion			
subjects affected / exposed	0 / 76 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease Progression			
subjects affected / exposed	0 / 76 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema Peripheral			

subjects affected / exposed	0 / 76 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 76 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic Reaction			
subjects affected / exposed	0 / 76 (0.00%)	2 / 77 (2.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylactic Shock			
subjects affected / exposed	1 / 76 (1.32%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug Hypersensitivity			
subjects affected / exposed	0 / 76 (0.00%)	3 / 77 (3.90%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	1 / 76 (1.32%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary Embolism			
subjects affected / exposed	0 / 76 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 76 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Depression			
subjects affected / exposed	0 / 76 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood Creatinine Increased			
subjects affected / exposed	1 / 76 (1.32%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases Increased			
subjects affected / exposed	0 / 76 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina Unstable			
subjects affected / exposed	1 / 76 (1.32%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Presyncope			
subjects affected / exposed	0 / 76 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 76 (1.32%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile Neutropenia			
subjects affected / exposed	2 / 76 (2.63%)	2 / 77 (2.60%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			

subjects affected / exposed	1 / 76 (1.32%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Eyelid Oedema			
subjects affected / exposed	0 / 76 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	1 / 76 (1.32%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal Pain Upper			
subjects affected / exposed	1 / 76 (1.32%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal Strangulated Hernia			
subjects affected / exposed	0 / 76 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 76 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 76 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal Reflux Disease			

subjects affected / exposed	1 / 76 (1.32%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal Haemorrhage			
subjects affected / exposed	0 / 76 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small Intestinal Perforation			
subjects affected / exposed	1 / 76 (1.32%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	1 / 76 (1.32%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	3 / 76 (3.95%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 76 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthropathy			
subjects affected / exposed	0 / 76 (0.00%)	1 / 77 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Staphylococcal Sepsis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 77 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Ombrabulin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	70 / 76 (92.11%)	73 / 77 (94.81%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 76 (3.95%)	5 / 77 (6.49%)	
occurrences (all)	3	8	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	20 / 76 (26.32%)	25 / 77 (32.47%)	
occurrences (all)	61	63	
Chills			
subjects affected / exposed	4 / 76 (5.26%)	0 / 77 (0.00%)	
occurrences (all)	7	0	
Fatigue			
subjects affected / exposed	13 / 76 (17.11%)	26 / 77 (33.77%)	
occurrences (all)	25	51	
Oedema Peripheral			
subjects affected / exposed	3 / 76 (3.95%)	4 / 77 (5.19%)	
occurrences (all)	3	4	
Pyrexia			
subjects affected / exposed	5 / 76 (6.58%)	10 / 77 (12.99%)	
occurrences (all)	13	11	
Immune system disorders			
Drug Hypersensitivity			
subjects affected / exposed	2 / 76 (2.63%)	8 / 77 (10.39%)	
occurrences (all)	2	10	
Hypersensitivity			

subjects affected / exposed occurrences (all)	6 / 76 (7.89%) 6	4 / 77 (5.19%) 7	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all) Epistaxis subjects affected / exposed occurrences (all)	1 / 76 (1.32%) 1 1 / 76 (1.32%) 1 4 / 76 (5.26%) 5	8 / 77 (10.39%) 10 6 / 77 (7.79%) 6 1 / 77 (1.30%) 2	
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) Anxiety subjects affected / exposed occurrences (all)	3 / 76 (3.95%) 4 4 / 76 (5.26%) 4	4 / 77 (5.19%) 5 3 / 77 (3.90%) 4	
Investigations Weight Decreased subjects affected / exposed occurrences (all)	3 / 76 (3.95%) 3	5 / 77 (6.49%) 6	
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Dysgeusia subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Neuropathy Peripheral subjects affected / exposed occurrences (all)	7 / 76 (9.21%) 8 4 / 76 (5.26%) 5 4 / 76 (5.26%) 8 14 / 76 (18.42%) 16	4 / 77 (5.19%) 5 3 / 77 (3.90%) 4 13 / 77 (16.88%) 31 15 / 77 (19.48%) 22	

Paraesthesia subjects affected / exposed occurrences (all)	4 / 76 (5.26%) 4	11 / 77 (14.29%) 16	
Peripheral Sensory Neuropathy subjects affected / exposed occurrences (all)	7 / 76 (9.21%) 7	10 / 77 (12.99%) 10	
Polyneuropathy subjects affected / exposed occurrences (all)	9 / 76 (11.84%) 11	8 / 77 (10.39%) 9	
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	9 / 76 (11.84%) 13	6 / 77 (7.79%) 6	
Neutropenia subjects affected / exposed occurrences (all)	25 / 76 (32.89%) 48	32 / 77 (41.56%) 74	
Thrombocytopenia subjects affected / exposed occurrences (all)	23 / 76 (30.26%) 55	23 / 77 (29.87%) 44	
Gastrointestinal disorders			
Abdominal Pain subjects affected / exposed occurrences (all)	19 / 76 (25.00%) 32	15 / 77 (19.48%) 20	
Abdominal Pain Upper subjects affected / exposed occurrences (all)	11 / 76 (14.47%) 22	11 / 77 (14.29%) 15	
Diarrhoea subjects affected / exposed occurrences (all)	21 / 76 (27.63%) 25	30 / 77 (38.96%) 70	
Constipation subjects affected / exposed occurrences (all)	18 / 76 (23.68%) 36	13 / 77 (16.88%) 38	
Dyspepsia subjects affected / exposed occurrences (all)	3 / 76 (3.95%) 4	4 / 77 (5.19%) 6	
Nausea			

subjects affected / exposed occurrences (all)	33 / 76 (43.42%) 89	32 / 77 (41.56%) 115	
Stomatitis subjects affected / exposed occurrences (all)	5 / 76 (6.58%) 7	5 / 77 (6.49%) 5	
Vomiting subjects affected / exposed occurrences (all)	24 / 76 (31.58%) 46	17 / 77 (22.08%) 35	
Skin and subcutaneous tissue disorders			
Alopecia subjects affected / exposed occurrences (all)	44 / 76 (57.89%) 44	48 / 77 (62.34%) 48	
Pruritus subjects affected / exposed occurrences (all)	7 / 76 (9.21%) 8	4 / 77 (5.19%) 5	
Erythema subjects affected / exposed occurrences (all)	1 / 76 (1.32%) 1	7 / 77 (9.09%) 10	
Rash subjects affected / exposed occurrences (all)	2 / 76 (2.63%) 2	5 / 77 (6.49%) 9	
Renal and urinary disorders			
Dysuria subjects affected / exposed occurrences (all)	4 / 76 (5.26%) 5	2 / 77 (2.60%) 6	
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	20 / 76 (26.32%) 57	26 / 77 (33.77%) 71	
Back Pain subjects affected / exposed occurrences (all)	4 / 76 (5.26%) 7	7 / 77 (9.09%) 14	
Bone Pain subjects affected / exposed occurrences (all)	3 / 76 (3.95%) 9	4 / 77 (5.19%) 4	
Myalgia			

subjects affected / exposed occurrences (all)	9 / 76 (11.84%) 12	20 / 77 (25.97%) 31	
Pain In Extremity subjects affected / exposed occurrences (all)	4 / 76 (5.26%) 7	5 / 77 (6.49%) 14	
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	2 / 76 (2.63%) 3	5 / 77 (6.49%) 6	
Respiratory Tract Infection Viral subjects affected / exposed occurrences (all)	5 / 76 (6.58%) 5	0 / 77 (0.00%) 0	
Urinary Tract Infection subjects affected / exposed occurrences (all)	2 / 76 (2.63%) 2	4 / 77 (5.19%) 6	
Metabolism and nutrition disorders Decreased Appetite subjects affected / exposed occurrences (all)	11 / 76 (14.47%) 18	9 / 77 (11.69%) 13	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 June 2011	Protocol amendment included following statement: For subject safety and further Afssaps request, minor change regarding exclusion criteria was done on the duration of contraception after the end of the treatment.
07 July 2011	A major change in exclusion criteria regarding QT/QTc was implemented. Subjects with QTc abnormalities during treatment could be withdrawn, after agreement between investigator and sponsor and one minor change is implemented regarding the timing of the first safety data review.
29 November 2011	It included following statements- To add the evaluation of the effect of ombrabulin on tumor volume and density as a secondary endpoint: Assessment of tumor response in clinical trial by RECIST might not be optimal for assessing the effect of a vascular disruptive agent (VDA) such as ombrabulin. Computer-aided volumetric analysis of target lesions could provide additional data to improve sensitivity and reproducibility over the RECIST criteria. The analysis of the effect of ombrabulin on tumor volume and density at different timepoints may help to better understand the activity of ombrabulin and ultimately might allow to propose a surrogate imaging biomarker. To clarify the conduct of the interim analysis and the distribution of its results

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported