Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Trial of Doxorubicin plus Olaratumab versus Doxorubicin plus Placebo in Patients with Advanced or Metastatic Soft Tissue Sarcoma

Summary

EudraCT number	2015-000134-30
Trial protocol	DK HU DE ES AT FR SE FI BE NL PL GB IT
Global end of trial date	27 June 2024

Results information

Result version number	v1 (current)
This version publication date	13 July 2025
First version publication date	13 July 2025

Trial information

Trial identification

Sponsor protocol code	I5B-MC-JGDJ

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02451943
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Name: ANNOUNCE

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Clinical Trial Registry Office, Eli Lilly , 1 08772854559, EU_Lilly_Clinical_Trials@lilly.com
Scientific contact	Clinical Trial Registry Office, Eli Lilly , 1 877CTLilly, EU_Lilly_Clinical_Trials@lilly.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	27 June 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 June 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to compare doxorubicin plus olaratumab versus doxorubicin plus placebo with respect to OS in 2 populations:
(1) Patients with advanced or metastatic soft tissue sarcoma (STS) not amenable to treatment with surgery or radiotherapy with curative intent
(2) Patients with advanced or metastatic leiomyosarcoma (LMS) not amenable to treatment with surgery or radiotherapy with curative intent

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -
Evidence for comparator: -

Actual start date of recruitment	28 August 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 14
Country: Number of subjects enrolled	Poland: 5
Country: Number of subjects enrolled	Spain: 34
Country: Number of subjects enrolled	Sweden: 7
Country: Number of subjects enrolled	United Kingdom: 26
Country: Number of subjects enrolled	Austria: 3
Country: Number of subjects enrolled	Belgium: 21
Country: Number of subjects enrolled	Denmark: 12
Country: Number of subjects enrolled	Finland: 6
Country: Number of subjects enrolled	France: 35
Country: Number of subjects enrolled	Germany: 16
Country: Number of subjects enrolled	Hungary: 20
Country: Number of subjects enrolled	Italy: 9
Country: Number of subjects enrolled	United States: 142
Country: Number of subjects enrolled	Russian Federation: 15
Country: Number of subjects enrolled	Korea, Republic of: 28

Country: Number of subjects enrolled	Brazil: 2
Country: Number of subjects enrolled	Argentina: 7
Country: Number of subjects enrolled	Japan: 45
Country: Number of subjects enrolled	Switzerland: 6
Country: Number of subjects enrolled	Canada: 18
Country: Number of subjects enrolled	Taiwan: 13
Country: Number of subjects enrolled	Mexico: 13
Country: Number of subjects enrolled	Israel: 11
Country: Number of subjects enrolled	Australia: 1
Worldwide total number of subjects	509
EEA total number of subjects	182

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)	360
From 65 to 84 years	149
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Completers include participants who died in the study.

Pre-assignment

Screening details:

NA

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	Doxorubicin + Olaratumab

Arm description:

75 milligrams per meter squared (mg/m^2) doxorubicin administered intravenously (IV) on day 1 of each 21 day cycle up to 8 cycles plus 20 milligrams per kilogram (mg/kg) dose of olaratumab administered IV on day 1 and day 8 of cycle 1 and 15 mg/kg olaratumab administered IV on day 1 and day 8 of cycles 2-8. 15 mg/kg olaratumab administered IV on day 1 and day 8 of each subsequent 21 day cycle thereafter until documented progressive disease (PD) or discontinuation for any other reason.

Arm type	Experimental
Investigational medicinal product name	Doxorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously.

Investigational medicinal product name	Olaratumab
Investigational medicinal product code	
Other name	LY3012207
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously.

Arm title	Doxorubicin + Placebo

Arm description:

75 mg/m^2 doxorubicin administered IV on day 1 of each 21 day cycle up to 8 cycles plus placebo (equivalent volume) administered IV on day 1 and day 8 for 8 cycles. Placebo (equivalent volume) administered on days 1 and 8 of each subsequent 21 day cycle thereafter until PD or discontinuation for any other reason.

Arm type	Placebo
Investigational medicinal product name	Doxorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details: Administered intravenously.	
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use
Dosage and administration details: Administered intravenously.	

Number of subjects in period 1	Doxorubicin + Olaratumab	Doxorubicin + Placebo
Started	258	251
Received at Least One Dose of Study Drug	257	249
Completed	242	227
Not completed	16	24
Consent withdrawn by subject	13	16
Sponsor Decision	-	4
Lost to follow-up	3	4

Baseline characteristics

Reporting groups	
Reporting group title	Doxorubicin + Olaratumab
Reporting group description:	
75 milligrams per meter squared (mg/m^2) doxorubicin administered intravenously (IV) on day 1 of each 21 day cycle up to 8 cycles plus 20 milligrams per kilogram (mg/kg) dose of olaratumab administered IV on day 1 and day 8 of cycle 1 and 15 mg/kg olaratumab administered IV on day 1 and day 8 of cycles 2-8. 15 mg/kg olaratumab administered IV on day 1 and day 8 of each subsequent 21 day cycle thereafter until documented progressive disease (PD) or discontinuation for any other reason.	
Reporting group title	Doxorubicin + Placebo
Reporting group description:	
75 mg/m^2 doxorubicin administered IV on day 1 of each 21 day cycle up to 8 cycles plus placebo (equivalent volume) administered IV on day 1 and day 8 for 8 cycles. Placebo (equivalent volume) administered on days 1 and 8 of each subsequent 21 day cycle thereafter until PD or discontinuation for any other reason.	

Reporting group values	Doxorubicin + Olaratumab	Doxorubicin + Placebo	Total
Number of subjects	258	251	509
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	56.7	57.1	
standard deviation	± 12.4	± 11.6	-
Gender categorical Units: Subjects			
Female	144	152	296
Male	114	99	213
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	26	29	55
Not Hispanic or Latino	209	199	408
Unknown or Not Reported	23	23	46
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	3	3	6
Asian	50	48	98
Native Hawaiian or Other Pacific Islander	1	0	1

Black or African American	12	2	14
White	186	193	379
More than one race	5	4	9
Unknown or Not Reported	1	1	2
Region of Enrollment Units: Subjects			
United States	69	73	142
Russia	7	8	15
Austria	3	0	3
South Korea	15	13	28
Netherlands	8	6	14
Sweden	4	3	7
Brazil	2	0	2
Poland	3	2	5
France	17	18	35
Argentina	3	4	7
Hungary	9	11	20
Japan	23	22	45
United Kingdom	10	16	26
Switzerland	4	2	6
Spain	13	21	34
Canada	12	6	18
Belgium	11	10	21
Finland	4	2	6
Taiwan	6	7	13
Denmark	10	2	12
Italy	5	4	9
Mexico	7	6	13
Israel	6	5	11
Australia	0	1	1
Germany	7	9	16

End points

End points reporting groups

Reporting group title	Doxorubicin + Olaratumab

Reporting group description:

75 milligrams per meter squared (mg/m^2) doxorubicin administered intravenously (IV) on day 1 of each 21 day cycle up to 8 cycles plus 20 milligrams per kilogram (mg/kg) dose of olaratumab administered IV on day 1 and day 8 of cycle 1 and 15 mg/kg olaratumab administered IV on day 1 and day 8 of cycles 2-8. 15 mg/kg olaratumab administered IV on day 1 and day 8 of each subsequent 21 day cycle thereafter until documented progressive disease (PD) or discontinuation for any other reason.

Reporting group title	Doxorubicin + Placebo

Reporting group description:

75 mg/m^2 doxorubicin administered IV on day 1 of each 21 day cycle up to 8 cycles plus placebo (equivalent volume) administered IV on day 1 and day 8 for 8 cycles. Placebo (equivalent volume) administered on days 1 and 8 of each subsequent 21 day cycle thereafter until PD or discontinuation for any other reason.

Primary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

Overall survival was defined as the time from the date of randomization to the date of death due to any cause. For each participant, prior to data analysis, a reasonable effort was made to obtain the most up-to-date status (date of death or last date known to be alive). For any participant not known to have died as of the data cutoff date, OS was censored at the date the participant was last known to be alive. For any participant who withdrew consent for survival follow-up, OS was censored at the last date for which the participant provided consent for follow-up contact. The Kaplan-Meier method was used to estimate median parameters.

Analysis Population Description (APD): All randomized participants. Censored participants in Doxorubicin + Olaratumab arm = 87 and Doxorubicin + Placebo arm = 91

End point type	Primary

End point timeframe:

Randomization to Date of Death Due to Any Cause (Up to 35.8 Months)

End point values	Doxorubicin + Olaratumab	Doxorubicin + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	258	251		
Units: Months				
median (confidence interval 95%)	20.37 (17.84 to 22.90)	19.75 (16.49 to 23.75)		

Statistical analyses

Statistical analysis title	Outcome Measure No. 1
Comparison groups	Doxorubicin + Olaratumab v Doxorubicin + Placebo

Number of subjects included in analysis	509
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6945
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.047
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.841
upper limit	1.303

Primary: Overall Survival (OS) Leiomyosarcoma (LMS)

End point title	Overall Survival (OS) Leiomyosarcoma (LMS)

End point description:

Overall survival was defined as the time from the date of randomization to the date of death due to any cause. For each participant, prior to data analysis, a reasonable effort was made to obtain the most up-to-date status (date of death or last date known to be alive). For any participant not known to have died as of the data cutoff date, OS was censored at the date the participant was last known to be alive. For any participant who withdrew consent for survival follow-up, OS was censored at the last date for which the participant provided consent for follow-up contact. The Kaplan-Meier method was used to estimate median parameters.

APD: All randomized participants with LMS. Censored participants in Doxorubicin + Olaratumab arm = 42 and Doxorubicin + Placebo arm = 40.

End point type	Primary

End point timeframe:

Randomization to Date of Death Due to Any Cause (Up to 35.8 Months)

End point values	Doxorubicin + Olaratumab	Doxorubicin + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	115		
Units: Months				
median (confidence interval 95%)	21.55 (18.63 to 27.63)	21.88 (17.54 to 25.07)		

Statistical analyses

Statistical analysis title	Outcome Measure No.2
Comparison groups	Doxorubicin + Olaratumab v Doxorubicin + Placebo

Number of subjects included in analysis	234
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7618
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.951
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.312

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)

End point description:

PFS was defined by (Response Evaluation Criteria In Solid Tumors RECIST v.1.1) as the time from the date of randomization to the first date of radiologic disease progression or death due to any cause. Progressive Disease (PD) is at least 20% increase in sum of diameters of target lesions, with reference being the smallest sum on study and plus absolute increase of at least 5 millimeter (mm), or unequivocal progression of non-target lesions, or 1 or more new lesions. Censoring for death or PD due to increase sum of target lesions is defined for each participant as the time from the date of randomization to the first date of radiographic documentation of 1 or more lesions. Censoring for death without progression is defined as the date of death if there is no prior or concurrent radiologic disease progression.

APD: All randomized participants. Censored participants in the Doxorubicin + Olaratumab arm = 39 and the Doxorubicin + Placebo arm =34.

End point type	Secondary

End point timeframe:

Randomization to Objective Progression or Death Due to Any Cause (Up to 35.8 Months)

End point values	Doxorubicin + Olaratumab	Doxorubicin + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	258	251		
Units: Months				
median (confidence interval 95%)	5.42 (4.11 to 6.70)	6.77 (5.49 to 8.08)		

Statistical analyses

Statistical analysis title	Outcome Measure No. 3
Comparison groups	Doxorubicin + Olaratumab v Doxorubicin + Placebo

Number of subjects included in analysis	509
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0422
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.231
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.009
upper limit	1.502

Secondary: Percentage of Participants Achieving Complete Response (CR) or Partial Response (PR): Objective Response Rate (ORR)

End point title	Percentage of Participants Achieving Complete Response (CR) or Partial Response (PR): Objective Response Rate (ORR)

End point description:

ORR was defined as the percentage of participants achieving a best overall response of complete response (CR) + partial response (PR). CR is the disappearance of all non-target lesions and normalization of tumor marker level. All lymph nodes must be non-pathological in size (<10 mm short axis). PR is at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. CR: Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm. Tumor marker results must have normalized. Best overall response is classified based on the overall responses assessed by study investigators according to RECIST v1.1.

APD: All randomized participants.

End point type	Secondary

End point timeframe:

Randomization to Objective Disease Progression or Death Due to Any Cause (Up to 35.8 Months)

End point values	Doxorubicin + Olaratumab	Doxorubicin + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	258	251		
Units: Percentage of participants				
number (confidence interval 95%)	14.0 (9.7 to 18.2)	18.3 (13.5 to 23.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With a Best Overall Response of CR, PR, or Stable Disease (SD): Disease Control Rate (DCR)

End point title	Percentage of Participants With a Best Overall Response of CR, PR, or Stable Disease (SD): Disease Control Rate (DCR)

End point description:

DCR was defined as the percentage of randomized participants achieving a best overall response of CR, PR, or SD per RECIST v.1.1. CR is the disappearance of all non-target lesions and normalization of tumor marker level. All lymph nodes must be non-pathological in size (<10 mm short axis). PR is at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. CR: Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm. Tumor marker results must have normalized. PD is at least 20% increase in sum of diameters of target lesions, with reference being the smallest sum on study and plus absolute increase of at least 5 mm, or unequivocal progression of non-target lesions, or 1 or more new lesions. SD: neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum diameters while on study.

End point type	Secondary

End point timeframe:

Randomization to Objective Disease Progression or Death Due to Any Cause (Up to 35.5 Months)

APD: All randomized participants.

End point values	Doxorubicin + Olaratumab	Doxorubicin + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	258	251		
Units: Percentage of participants				
number (confidence interval 95%)	67.4 (61.7 to 73.2)	75.7 (70.4 to 81.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Worsening on the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) Scores

End point title	Time to First Worsening on the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) Scores

End point description:

Time to first worsening was calculated as the time from the first study drug dose to the first observation of worsening according to the EORTC QLQ-C30 Scoring Manual (Fayers et al. 2001). The EORTC QLQ-C30 self-reported general cancer instrument consists of 30 total items covered by 1 of 3 dimensions (1 global health status/QoL total score, 5 functional subscales [physical, role, cognitive, emotional, and social]), and 9 symptom subscales [fatigue/nausea/vomiting/pain/dyspnea/insomnia/appetite loss/constipation/diarrhea]). There are 28 questions answered on a 4-point scale where 1=Not at all (best) to 4=Very Much (worst) and 2 questions answered on a 7-point scale where 1=Very poor (worst) to 7= Excellent (best). A linear transformation was used to obtain total score ranging from 0 to 100 where "worsening" was defined as an increase of at least 10 points for the symptom scales or a decrease of at least 10 points for the functional scales and the global health status/QoL scale.

End point type	Secondary

End point timeframe:

Randomization (Cycle 1) through Follow-up (Up to 35.8 Months)

APD: All randomized participants who completed at least 1 baseline assessment and at least 1 subsequent assessment during the study period.

End point values	Doxorubicin + Olaratumab	Doxorubicin + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	201	197		
Units: Months				
median (confidence interval 95%)				
Role Functional Scale (n=202;190)	1.41 (0.99 to 1.48)	1.41 (0.954 to 2.00)		
Global Health Status/QoL (n=201;197)	1.45 (1.41 to 2.10)	1.84 (1.45 to 2.79)		
Physical Functional Scale (n=205;209)	1.81 (1.45 to 2.14)	2.79 (2.07 to 3.48)		
Emotional Functional Scale (n=168;171)	3.48 (2.50 to 4.37)	2.83 (2.14 to 4.34)		
Cognitive Functional Scale (n=170;167)	1.64 (1.41 to 2.14)	1.45 (1.41 to 2.07)		
Social Functional Scale (n=189;171)	1.45 (1.38 to 1.64)	1.41 (1.35 to 1.45)		
Fatigue Symptom Scale (n=210;204)	0.92 (0.76 to 1.25)	0.89 (0.76 to 1.38)		
Nausea and Vomiting Symptom Scale (n=182;173)	1.45 (1.41 to 1.64)	1.41 (0.95 to 1.45)		
Pain Symptom Scale (n=185;183)	1.64 (1.41 to 2.10)	2.10 (1.45 to 2.76)		
Dyspnea Symptom Scale (n= 158;160)	2.10 (1.45 to 2.76)	2.07 (1.45 to 2.79)		
Insomnia Symptom Scale (n=151;160)	2.10 (1.45 to 2.79)	1.58 (1.41 to 2.33)		
Appetite Loss Symptom Scale (n=182;170)	1.48 (1.45 to 2.04)	1.64 (1.41 to 2.14)		
Financial Difficulties Scale (n=132;105)	1.48 (1.41 to 2.14)	1.45 (1.41 to 2.10)		
Constipation Symptom Scale (n=169;157)	1.64 (1.41 to 2.10)	1.41 (1.41 to 2.10)		
Diarrhea Symptom Scale (n=157;148)	2.07 (1.45 to 2.79)	2.79 (2.10 to 3.52)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Maximum Improvement in Health Status Index Score on the EuroQol 5-Dimension 5-Level (EQ-5D-5L)

End point title	Change From Baseline to Maximum Improvement in Health Status Index Score on the EuroQol 5-Dimension 5-Level (EQ-5D-5L)

End point description:

The EQ-5D-5L is a standardized measure of health status used to provide a simple, generic measure of health for clinical and economic appraisal. The EQ-5D-5L consists of a descriptive system of the respondent's health which comprises the following 5 dimensions: (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression). Health status was calculated from a set of item weights to derive a score of 0 to 1, with 1 representing the best health status. United Kingdom (UK) weights were applied. The analysis includes all cycles for which at least 25% of participants in each arm have an

assessment. For each participant a change from baseline was calculated for every post-baseline assessment by subtracting the baseline assessment result from the current assessment result. Maximum improvement (over baseline) was determined from the set of all post-baseline change scores.

APD: All randomized participants who had a baseline and a post-baseline measurement.

End point type	Secondary

End point timeframe:

Randomization through Follow-up (Up to 35.8 Months)

End point values	Doxorubicin + Olaratumab	Doxorubicin + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	221	219		
Units: Score on a scale				
arithmetic mean (standard deviation)	-0.163 (± 0.236)	-0.171 (± 0.235)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Worsening of the Brief Pain Inventory Short Form Modified (mBPI-sf) "Worst Pain Score"

End point title	Time to First Worsening of the Brief Pain Inventory Short Form Modified (mBPI-sf) "Worst Pain Score"

End point description:

Time to first worsening of the brief pain inventory short form modified (mBPI-sf) "worst pain score" was defined as the time from the date of the first study drug dose (baseline date) to the first date of a "worst pain" score increase of greater than or equal to (≥) 2 points from baseline. The mBPI-sf is an 11-item instrument used as a multiple-item measure of cancer pain intensity ranging from 0 (no pain or does not interfere) and ranged through 10 (pain as bad as you can imagine or completely interferes).

APD: All randomized participants who completed at least 1 baseline assessment and at least 1 subsequent assessment during the study period.

End point type	Secondary

End point timeframe:

Randomization through Follow-up (Up to 34.5 Months)

End point values	Doxorubicin + Olaratumab	Doxorubicin + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	211	206		
Units: Months				
median (confidence interval 95%)	7.66 (6.01 to 9.63)	8.08 (6.18 to 11.07)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Overall Response (DoR)

End point title	Duration of Overall Response (DoR)

End point description:

The duration of overall response was defined for each participant with a best response of CR or PR and measured from the time measurement criteria are first met for CR or PR (whichever is first recorded) until the first date that disease is recurrent or objective disease progression or death due to any cause is observed (taking as reference for PD the smallest measurements recorded on study).

APD: All randomized participants who have evaluable DoR data.

End point type	Secondary

End point timeframe:

Date of CR or PR to Date of Objective Disease Progression or Death Due to Any Cause (Up to 33.4 Months)

End point values	Doxorubicin + Olaratumab	Doxorubicin + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	46		
Units: Months				
median (confidence interval 95%)	8.31 (6.87 to 12.35)	4.80 (3.65 to 6.83)		

Statistical analyses

Statistical analysis title	Outcome Measure No. 9
Comparison groups	Doxorubicin + Olaratumab v Doxorubicin + Placebo
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0934
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.616
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.347
upper limit	1.093

Secondary: Duration of Disease Control (DDC)

End point title	Duration of Disease Control (DDC)

End point description:

Duration of disease control was defined for each participant with a best response of CR, PR, or stable disease (SD) as the time from randomization to the first date of disease progression or death due to any cause.

APD: All randomized participants who had evaluable DDC data.

End point type	Secondary

End point timeframe:

Date of CR, PR, or SD to Objective Disease Progression or Death Due to Any Cause (Up to 35.8 Months)

End point values	Doxorubicin + Olaratumab	Doxorubicin + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	174	190		
Units: Months				
median (confidence interval 95%)	8.28 (6.93 to 9.72)	8.34 (8.08 to 9.46)		

Statistical analyses

Statistical analysis title	Outcome Measure No. 10
Comparison groups	Doxorubicin + Olaratumab v Doxorubicin + Placebo
Number of subjects included in analysis	364
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3347
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.123
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.892
upper limit	1.413

Secondary: Pharmacokinetics (PK) Clearance of Olaratumab Mean Parameter Estimate

End point title	Pharmacokinetics (PK) Clearance of Olaratumab Mean Parameter Estimate[1]

End point description:

The PK systemic clearance parameter estimates from the current analysis are listed together with the population PK model estimates.

APD: All randomized participants who received at least one dose of study drug and had evaluable PK data.

End point type	Secondary

End point timeframe:

Cycle 1- 9: Day 1 and 8, Predose, 5 minutes Post dose and then every other cycle and follow-up (30 Days)

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: All randomized participants who received at least one dose of olaratumab and had evaluable PK data were involved in this analysis.

End point values	Doxorubicin + Olaratumab			
Subject group type	Reporting group			
Number of subjects analysed	258			
Units: Liter/hour (L/h)				
arithmetic mean (confidence interval 95%)	0.0195 (0.0189 to 0.0203)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK: Volume of Distribution at Steady State (Vss) of Olaratumab: Mean Parameter Estimate

End point title	PK: Volume of Distribution at Steady State (Vss) of Olaratumab: Mean Parameter Estimate[2]

End point description:

The PK parameter estimates from the current analysis are listed together with the population PK model estimates. The Vss is the sum of central volume of distribution (V1) + peripheral volume of distribution (V2).

APD: All randomized participants who had received at least one dose of study drug and had evaluable PK data.

End point type	Secondary

End point timeframe:

Cycle 1- 9: Day 1 and 8; Predose, 5 Minutes Post dose and then every other cycle and follow-up (30 Days)

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: All randomized participants who received at least one dose of olaratumab and had evaluable PK data were involved in this analysis.

End point values	Doxorubicin + Olaratumab			
Subject group type	Reporting group			
Number of subjects analysed	258			
Units: Liter (L)				
arithmetic mean (confidence interval 95%)	5.72 (5.28 to 6.17)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline Up To 41 Months

Adverse event reporting additional description:

All participants who received at least one dose of study drug. Gender specific events occurring only in male or female participants have had the number of participants at risk adjusted accordingly. Based on the planned safety analysis, adverse event analysis was planned as per the treatments the participants received.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	28.0

Reporting groups

Reporting group title	Doxorubicin + Placebo

Reporting group description:

75 mg/m^2 doxorubicin administered IV on day 1 of each 21 day cycle for 8 cycles plus placebo (equivalent volume) administered IV on day 1 and day 8 for 8 cycles. Beginning with cycle 9, placebo (equivalent volume) administered on days 1 and 8 of each subsequent 21 day cycle until PD or discontinuation for any other reason.

Reporting group title	Doxorubicin + Olaratumab

Reporting group description:

75 milligrams per meter squared (mg/m^2) doxorubicin administered intravenously (IV) on day 1 of each 21 day cycle for 8 cycles plus 20 milligrams per kilogram (mg/kg) dose of olaratumab administered IV on day 1 and day 8 of cycle 1 and 15 mg/kg olaratumab administered IV on day 1 and day 8 of cycles 2-8. Beginning with cycle 9, 15 mg/kg olaratumab administered IV on day 1 and day 8 of each subsequent 21 day cycle until documented progressive disease (PD) or discontinuation for any other reason.

Serious adverse events	Doxorubicin + Placebo	Doxorubicin + Olaratumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	89 / 249 (35.74%)	105 / 257 (40.86%)	
number of deaths (all causes)	158	170	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
adenocarcinoma of colon			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
deep vein thrombosis			
alternative dictionary used: MedDRA 28.0			

subjects affected / exposed	1 / 249 (0.40%)	5 / 257 (1.95%)	
occurrences causally related to treatment / all	0 / 1	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
embolism			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypotension			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	2 / 257 (0.78%)	
occurrences causally related to treatment / all	1 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
peripheral arterial occlusive disease			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
superficial vein thrombosis			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
venous thrombosis			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 28.0			

subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
extravasation			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
fatigue			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
malaise			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
mucosal inflammation			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
non-cardiac chest pain			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pyrexia			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	7 / 249 (2.81%)	2 / 257 (0.78%)	
occurrences causally related to treatment / all	3 / 7	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Immune system disorders			
anaphylactic reaction			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	2 / 257 (0.78%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
anaphylactic shock			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypersensitivity			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
vaginal haemorrhage			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed[1]	1 / 151 (0.66%)	0 / 144 (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			
acute respiratory failure			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
aspiration			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	

chronic obstructive pulmonary disease			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
dyspnoea			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypoxia			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pleural effusion			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pulmonary embolism			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	3 / 249 (1.20%)	7 / 257 (2.72%)	
occurrences causally related to treatment / all	2 / 3	2 / 7	
deaths causally related to treatment / all	0 / 0	1 / 2	
pneumothorax			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	3 / 249 (1.20%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	1 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonitis			
alternative dictionary used: MedDRA 28.0			

subjects affected / exposed	1 / 249 (0.40%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
respiratory failure			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
anxiety			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
ejection fraction decreased			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
electrocardiogram abnormal			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
neutrophil count decreased			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	4 / 249 (1.61%)	5 / 257 (1.95%)	
occurrences causally related to treatment / all	4 / 7	5 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
platelet count decreased			
alternative dictionary used: MedDRA 28.0			

subjects affected / exposed	2 / 249 (0.80%)	2 / 257 (0.78%)	
occurrences causally related to treatment / all	2 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
troponin increased			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
white blood cell count decreased			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	3 / 249 (1.20%)	2 / 257 (0.78%)	
occurrences causally related to treatment / all	3 / 4	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
femur fracture			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
femoral neck fracture			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
rib fracture			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
spinal fracture			
alternative dictionary used: MedDRA 28.0			

subjects affected / exposed	2 / 249 (0.80%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
tibia fracture			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
arrhythmia			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
atrial fibrillation			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	2 / 257 (0.78%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
cardiac failure congestive			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	2 / 249 (0.80%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
cardiac failure acute			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
cardiac failure			
alternative dictionary used: MedDRA 28.0			

subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
left ventricular dysfunction			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	2 / 257 (0.78%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
mitral valve disease			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
myocarditis			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pericarditis			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
supraventricular tachycardia			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
cerebrovascular accident			
alternative dictionary used: MedDRA 28.0			

subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
dysarthria			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
headache			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ischaemic stroke			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
migraine			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
nervous system disorder			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
paraparesis			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

sciatic nerve neuropathy			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
somnolence			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
syncope			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
vertebrobasilar artery dissection			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
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			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	2 / 249 (0.80%)	4 / 257 (1.56%)	
occurrences causally related to treatment / all	2 / 2	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
febrile bone marrow aplasia			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
febrile neutropenia			
alternative dictionary used: MedDRA 28.0			

subjects affected / exposed	33 / 249 (13.25%)	34 / 257 (13.23%)	
occurrences causally related to treatment / all	33 / 37	34 / 37	
deaths causally related to treatment / all	0 / 0	0 / 0	
leukopenia			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
neutropenia			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	8 / 249 (3.21%)	8 / 257 (3.11%)	
occurrences causally related to treatment / all	8 / 8	8 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
pancytopenia			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
thrombocytopenia			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	2 / 249 (0.80%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	2 / 5	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
acute abdomen			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
abdominal pain			
alternative dictionary used: MedDRA 28.0			

subjects affected / exposed	2 / 249 (0.80%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
constipation			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
colitis			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
diarrhoea			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	3 / 257 (1.17%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
duodenal ulcer			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
dyspepsia			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
food poisoning			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

gastric haemorrhage			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ileus			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	2 / 249 (0.80%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
intestinal obstruction			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
intussusception			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
nausea			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	4 / 257 (1.56%)	
occurrences causally related to treatment / all	0 / 0	3 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
small intestinal obstruction			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
subileus			
alternative dictionary used: MedDRA 28.0			

subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
stomatitis			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	2 / 249 (0.80%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	2 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
vomiting			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	4 / 257 (1.56%)	
occurrences causally related to treatment / all	1 / 1	3 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
hepatic pain			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
acute kidney injury			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
nephrolithiasis			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
renal failure			
alternative dictionary used: MedDRA 28.0			

subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
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			
arthralgia			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	4 / 257 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
back pain			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
intervertebral disc protrusion			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pathological fracture			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	2 / 257 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
abdominal infection			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
abscess			
alternative dictionary used: MedDRA 28.0			

subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
bacteraemia			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
cellulitis			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	2 / 249 (0.80%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
cystitis			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
clostridium difficile colitis			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
device related infection			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	2 / 257 (0.78%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
gingivitis			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

gastroenteritis			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
herpes zoster			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
infection			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	2 / 257 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
neutropenic sepsis			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
neutropenic infection			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pseudomonal bacteraemia			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonia aspiration			
alternative dictionary used: MedDRA 28.0			

subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonia			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	2 / 249 (0.80%)	4 / 257 (1.56%)	
occurrences causally related to treatment / all	0 / 2	2 / 4	
deaths causally related to treatment / all	0 / 0	1 / 2	
sepsis			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	2 / 249 (0.80%)	4 / 257 (1.56%)	
occurrences causally related to treatment / all	1 / 2	3 / 4	
deaths causally related to treatment / all	0 / 1	0 / 0	
respiratory tract infection			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
rectal abscess			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
septic shock			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
skin infection			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

upper respiratory tract infection			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
urinary tract infection			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	3 / 257 (1.17%)	
occurrences causally related to treatment / all	1 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
tonsillitis			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
wound infection			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
dehydration			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypoglycaemia			
alternative dictionary used: MedDRA 28.0			

subjects affected / exposed	0 / 249 (0.00%)	1 / 257 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypokalaemia			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hyperglycaemia			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	1 / 249 (0.40%)	0 / 257 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Gender specific events occurring only in male or female participants have had the number of participants at risk adjusted accordingly.

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

Non-serious adverse events	Doxorubicin + Placebo	Doxorubicin + Olaratumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	244 / 249 (97.99%)	248 / 257 (96.50%)	
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	21 / 249 (8.43%)	20 / 257 (7.78%)	
occurrences (all)	33	29	
aspartate aminotransferase increased			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	20 / 249 (8.03%)	11 / 257 (4.28%)	
occurrences (all)	28	12	
gamma-glutamyltransferase increased			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	19 / 249 (7.63%)	21 / 257 (8.17%)	
occurrences (all)	25	25	

lymphocyte count decreased			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	17 / 249 (6.83%)	17 / 257 (6.61%)	
occurrences (all)	39	47	
neutrophil count decreased			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	90 / 249 (36.14%)	92 / 257 (35.80%)	
occurrences (all)	256	205	
platelet count decreased			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	46 / 249 (18.47%)	47 / 257 (18.29%)	
occurrences (all)	140	122	
weight decreased			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	23 / 249 (9.24%)	25 / 257 (9.73%)	
occurrences (all)	25	26	
white blood cell count decreased			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	69 / 249 (27.71%)	68 / 257 (26.46%)	
occurrences (all)	181	177	
Vascular disorders			
hypertension			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	24 / 249 (9.64%)	19 / 257 (7.39%)	
occurrences (all)	31	23	
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	35 / 249 (14.06%)	27 / 257 (10.51%)	
occurrences (all)	49	44	
dysgeusia			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	47 / 249 (18.88%)	42 / 257 (16.34%)	
occurrences (all)	57	50	
headache			

alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	42 / 249 (16.87%)	43 / 257 (16.73%)	
occurrences (all)	56	61	
paraesthesia			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	16 / 249 (6.43%)	12 / 257 (4.67%)	
occurrences (all)	17	15	
General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	30 / 249 (12.05%)	24 / 257 (9.34%)	
occurrences (all)	66	42	
fatigue			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	133 / 249 (53.41%)	129 / 257 (50.19%)	
occurrences (all)	211	181	
malaise			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	15 / 249 (6.02%)	11 / 257 (4.28%)	
occurrences (all)	20	13	
oedema peripheral			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	25 / 249 (10.04%)	37 / 257 (14.40%)	
occurrences (all)	39	44	
pyrexia			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	42 / 249 (16.87%)	50 / 257 (19.46%)	
occurrences (all)	61	65	
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	121 / 249 (48.59%)	115 / 257 (44.75%)	
occurrences (all)	230	169	
febrile neutropenia			
alternative dictionary used:			

MedDRA 28.0			
subjects affected / exposed	9 / 249 (3.61%)	13 / 257 (5.06%)	
occurrences (all)	12	13	
leukopenia			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	11 / 249 (4.42%)	14 / 257 (5.45%)	
occurrences (all)	23	36	
neutropenia			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	59 / 249 (23.69%)	59 / 257 (22.96%)	
occurrences (all)	121	131	
thrombocytopenia			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	19 / 249 (7.63%)	14 / 257 (5.45%)	
occurrences (all)	35	29	
Gastrointestinal disorders			
abdominal pain			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	44 / 249 (17.67%)	31 / 257 (12.06%)	
occurrences (all)	55	43	
abdominal pain upper			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	20 / 249 (8.03%)	17 / 257 (6.61%)	
occurrences (all)	23	23	
constipation			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	94 / 249 (37.75%)	86 / 257 (33.46%)	
occurrences (all)	144	122	
diarrhoea			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	76 / 249 (30.52%)	79 / 257 (30.74%)	
occurrences (all)	118	123	
dry mouth			
alternative dictionary used: MedDRA 28.0			

subjects affected / exposed	19 / 249 (7.63%)	22 / 257 (8.56%)	
occurrences (all)	21	23	
gastrooesophageal reflux disease alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	18 / 249 (7.23%)	16 / 257 (6.23%)	
occurrences (all)	19	17	
dyspepsia alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	29 / 249 (11.65%)	28 / 257 (10.89%)	
occurrences (all)	34	33	
nausea alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	171 / 249 (68.67%)	154 / 257 (59.92%)	
occurrences (all)	369	293	
stomatitis alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	93 / 249 (37.35%)	79 / 257 (30.74%)	
occurrences (all)	167	134	
vomiting alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	70 / 249 (28.11%)	62 / 257 (24.12%)	
occurrences (all)	128	78	
Respiratory, thoracic and mediastinal disorders			
cough alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	66 / 249 (26.51%)	46 / 257 (17.90%)	
occurrences (all)	81	54	
epistaxis alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	13 / 249 (5.22%)	7 / 257 (2.72%)	
occurrences (all)	19	7	
dyspnoea alternative dictionary used: MedDRA 28.0			

subjects affected / exposed	39 / 249 (15.66%)	46 / 257 (17.90%)	
occurrences (all)	48	53	
oropharyngeal pain			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	19 / 249 (7.63%)	16 / 257 (6.23%)	
occurrences (all)	25	20	
Skin and subcutaneous tissue disorders			
alopecia			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	127 / 249 (51.00%)	113 / 257 (43.97%)	
occurrences (all)	132	116	
dry skin			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	11 / 249 (4.42%)	15 / 257 (5.84%)	
occurrences (all)	11	15	
pruritus			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	23 / 249 (9.24%)	15 / 257 (5.84%)	
occurrences (all)	26	16	
rash			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	18 / 249 (7.23%)	13 / 257 (5.06%)	
occurrences (all)	20	16	
Psychiatric disorders			
anxiety			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	16 / 249 (6.43%)	17 / 257 (6.61%)	
occurrences (all)	17	21	
insomnia			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	34 / 249 (13.65%)	25 / 257 (9.73%)	
occurrences (all)	39	29	
Musculoskeletal and connective tissue disorders			

back pain			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	31 / 249 (12.45%)	35 / 257 (13.62%)	
occurrences (all)	38	48	
arthralgia			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	22 / 249 (8.84%)	32 / 257 (12.45%)	
occurrences (all)	27	40	
myalgia			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	12 / 249 (4.82%)	13 / 257 (5.06%)	
occurrences (all)	13	20	
muscle spasms			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	8 / 249 (3.21%)	18 / 257 (7.00%)	
occurrences (all)	9	25	
pain in extremity			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	27 / 249 (10.84%)	29 / 257 (11.28%)	
occurrences (all)	40	37	
Infections and infestations			
nasopharyngitis			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	16 / 249 (6.43%)	10 / 257 (3.89%)	
occurrences (all)	17	12	
rhinitis			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	13 / 249 (5.22%)	6 / 257 (2.33%)	
occurrences (all)	16	6	
upper respiratory tract infection			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	25 / 249 (10.04%)	25 / 257 (9.73%)	
occurrences (all)	30	31	
urinary tract infection			
alternative dictionary used: MedDRA 28.0			

subjects affected / exposed	23 / 249 (9.24%)	20 / 257 (7.78%)	
occurrences (all)	28	29	
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	93 / 249 (37.35%)	74 / 257 (28.79%)	
occurrences (all)	131	108	
dehydration			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	9 / 249 (3.61%)	18 / 257 (7.00%)	
occurrences (all)	13	24	
hyperglycaemia			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	10 / 249 (4.02%)	13 / 257 (5.06%)	
occurrences (all)	14	21	
hypokalaemia			
alternative dictionary used: MedDRA 28.0			
subjects affected / exposed	14 / 249 (5.62%)	14 / 257 (5.45%)	
occurrences (all)	18	18	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 May 2015	• Leiomyosarcoma (LMS) was added as a specific population to be tested within the primary objective, and is now co-primary with the STS (ITT) population. • Pleomorphic was added to the stratifications factors • Due to regional/institutional differences dexrazoxane dosing was modified • PFS2 was added to the efficacy endpoints • Cardiovascular monitoring was increased • Gatekeeping methods have been included for OS, PFS, ORR, and DoR • Grade 1 liposarcoma patients are now included under certain conditions • The olaratumab dosing regimen was modified • Management of infusion-related reactions was modified • Single interim analysis will be performed based on 60% of overall OS events (194) in the ITT population and 72 events from the LMS • Analysis of OS will be based on the stratified log-rank test analyzed by the randomization strata, excluding region.
04 January 2016	• Some exclusion criteria were deleted • Grade 4 nonhematologic toxicity as related to study therapy is now considered a basis for study drug discontinuation • Duration of Response was deleted from secondary objectives. • O'Brien-Fleming alpha spending will now be used for all efficacy boundaries • bisphosphonate osteoclast inhibitors are now allowed, denosumab is still not permitted.
22 January 2016	• Germany was directed to refer to Addendum (7)
12 January 2017	• Patients receiving anticoagulants are now eligible to participate • Long-term follow-up for survival and patient reported outcome collection were updated so that these events are concurrent with the collection of ECG data • Efficacy interim stopping rules were removed from the protocol plan, as the intention is to continue the study until the final analysis with the sponsor remaining blinded to aggregate data by study arm until the final analysis. • Urine protein creatinine ratio of spot urine can now be used in place of 24-hour urine protein excretion.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported