Clinical trial results:
A Study of Liposomal Doxorubicin With or Without Olaratumab (IMC-3G3) in Platinum-Refractory or Resistant Advanced Ovarian Cancer

Summary

EudraCT number	2009-009035-30
Trial protocol	GB
Global end of trial date	13 February 2014

Results information

Result version number	v1 (current)
This version publication date	04 December 2016
First version publication date	04 December 2016

Trial information

Trial identification

Sponsor protocol code	13899

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00913835
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 13899, Trial Alias: I5B-IE-JGDA

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company , 1 877-CTLilly,
Scientific contact	Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company , 1 877-285-4559,

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	13 February 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 February 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to determine if participants with platinum-refractory or platinum-resistant advanced ovarian cancer have a better outcome when treated with Olaratumab (IMC-3G3) in combination with Liposomal Doxorubicin than when treated with Liposomal Doxorubicin alone.

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	11 June 2009
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	United States: 75
Country: Number of subjects enrolled	United Kingdom: 31
Country: Number of subjects enrolled	Spain: 19
Worldwide total number of subjects	125
EEA total number of subjects	50

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)	90
From 65 to 84 years	35

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

No Text Entered

Pre-assignment

Screening details:

Participants from liposomal doxorubicin (Lip Dox) treatment group who had progressive disease (PD) had the option to receive to Olaratumab (Olara) monotherapy. Participants who had evidence of PD, died in either period, or received optional Olaratumab monotherapy from liposomal doxorubicin monotherapy were considered to have completed the study.

Period 1

Period 1 title	Olara+Lip Dox and Lip Dox Monotherapy
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Olaratumab + Liposomal Doxorubicin

Arm description:

20 milligrams per kilogram (mg/kg) of Olaratumab was administered as an intravenous (IV) infusion every 2 weeks (14 days) until there was evidence of progressive disease (PD) or development of unacceptable toxicity.

40 milligrams per square meter (mg/m²) of liposomal doxorubicin was administered according to the manufacturer's instructions every 4 weeks (28 days) until there was evidence of PD or development of unacceptable toxicity.

Arm type	Experimental
Investigational medicinal product name	Olaratumab
Investigational medicinal product code	
Other name	IMC-3G3, LY3012207
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

20 milligrams per kilogram (mg/kg) of Olaratumab was administered as an intravenous (IV) infusion every 2 weeks (14 days) until there was evidence of progressive disease (PD) or development of unacceptable toxicity.

Investigational medicinal product name	Liposomal Doxorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

40 milligrams per square meter (mg/m²) of liposomal doxorubicin was administered according to the manufacturer's instructions every 4 weeks (28 days) until there was evidence of PD or development of unacceptable toxicity.

Arm title	Liposomal Doxorubicin

Arm description:

40 mg/m² of liposomal doxorubicin was administered according to the manufacturer's instructions every 4 weeks (28 days). Treatment continued until there is evidence of PD or development of unacceptable toxicity up to 130 weeks.

Upon disease progression the participant had the option to receive Olaratumab monotherapy.

Arm type	Active comparator
Investigational medicinal product name	Liposomal Doxorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

40 mg/m² of liposomal doxorubicin was administered according to the manufacturer's instructions every 4 weeks (28 days). Treatment continued until there is evidence of PD or development of unacceptable toxicity up to 130 weeks.

Number of subjects in period 1	Olaratumab + Liposomal Doxorubicin	Liposomal Doxorubicin
Started	63	62
Received Any Study Drug	62	61
Completed	55	55
Not completed	8	7
Consent withdrawn by subject	2	3
Not Specified	4	3
Lost to follow-up	1	-
Off Study Treatment/Alive	1	1

Period 2

Period 2 title	Lip Dox: Olaratumab Monotherapy
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Optional Olaratumab Monotherapy

Arm description:

20 milligrams per kilogram (mg/kg) of Olaratumab was administered as an intravenous (IV) infusion every 2 weeks (14 days) until there was evidence of progressive disease (PD) or development of unacceptable toxicity.

Arm type	Experimental
Investigational medicinal product name	Olaratumab
Investigational medicinal product code	
Other name	IMC-3G3, LY3012207
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

20 milligrams per kilogram (mg/kg) of Olaratumab was administered as an intravenous (IV) infusion every 2 weeks (14 days) until there was evidence of progressive disease (PD) or development of unacceptable toxicity.

Number of subjects in period 2[1]	Optional Olaratumab Monotherapy
Started	28
Received at least 1 dose of study drug	28
Completed	25
Not completed	3
Not Specified	3

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Participants from liposomal doxorubicin (Lip Dox) treatment group who had progressive disease (PD) had the option to receive to Olaratumab (Olara) monotherapy.

Baseline characteristics

Reporting groups	
Reporting group title	Olaratumab + Liposomal Doxorubicin

Reporting group description:

20 milligrams per kilogram (mg/kg) of Olaratumab was administered as an intravenous (IV) infusion every 2 weeks (14 days) until there was evidence of progressive disease (PD) or development of unacceptable toxicity.

40 milligrams per square meter (mg/m²) of liposomal doxorubicin was administered according to the manufacturer's instructions every 4 weeks (28 days) until there was evidence of PD or development of unacceptable toxicity.

Reporting group title	Liposomal Doxorubicin

Reporting group description:

40 mg/m² of liposomal doxorubicin was administered according to the manufacturer's instructions every 4 weeks (28 days). Treatment continued until there is evidence of PD or development of unacceptable toxicity up to 130 weeks.

Upon disease progression the participant had the option to receive Olaratumab monotherapy.

Reporting group values	Olaratumab + Liposomal Doxorubicin	Liposomal Doxorubicin	Total
Number of subjects	63	62	125
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	47	43	90
From 65-84 years	16	19	35
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	58.7	59.8	
standard deviation	± 10.07	± 9.7	-
Gender, Male/Female Units: participants			
Female	63	62	125
Male	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	6	7
Not Hispanic or Latino	62	55	117
Unknown or Not Reported	0	1	1
Race/Ethnicity, Customized Units: Subjects			
Asian	1	3	4

Black or African American	5	1	6
Native Hawaiian of Other Pacific Islander	0	1	1
White	55	55	110
Other	2	2	4
Region of Enrollment Units: Subjects			
United States	41	34	75
United Kingdom	17	14	31
Spain	5	14	19
Eastern Cooperative Oncology Group (ECOG) Performance Status (PS)			
ECOG PS classified participants according to their functional impairment.			
Units: Subjects			
0-Fully Active	38	32	70
1-ambulatory, able to do light/sedentary nature	25	30	55
Stratification Factor			
Participants reaction to prior platinum treatment.			
Units: Subjects			
Platinum Refractory	16	15	31
Platinum Resistant	47	47	94

End points

End points reporting groups

Reporting group title	Olaratumab + Liposomal Doxorubicin

Reporting group description:

20 milligrams per kilogram (mg/kg) of Olaratumab was administered as an intravenous (IV) infusion every 2 weeks (14 days) until there was evidence of progressive disease (PD) or development of unacceptable toxicity.

40 milligrams per square meter (mg/m²) of liposomal doxorubicin was administered according to the manufacturer's instructions every 4 weeks (28 days) until there was evidence of PD or development of unacceptable toxicity.

Reporting group title	Liposomal Doxorubicin

Reporting group description:

40 mg/m² of liposomal doxorubicin was administered according to the manufacturer's instructions every 4 weeks (28 days). Treatment continued until there is evidence of PD or development of unacceptable toxicity up to 130 weeks.

Upon disease progression the participant had the option to receive Olaratumab monotherapy.

Reporting group title	Optional Olaratumab Monotherapy

Reporting group description:

20 milligrams per kilogram (mg/kg) of Olaratumab was administered as an intravenous (IV) infusion every 2 weeks (14 days) until there was evidence of progressive disease (PD) or development of unacceptable toxicity.

Subject analysis set title	Olaratumab and Liposomal Doxorubicin
Subject analysis set type	Full analysis

Subject analysis set description:

20 mg/kg of Olaratumab was administered as an IV infusion every 2 weeks (14 days) until there was evidence of PD or development of unacceptable toxicity up to 130 weeks.

40 mg/m² of liposomal doxorubicin was administered according to the manufacturer's instructions every 4 weeks (28 days) until there was evidence of PD or development of unacceptable toxicity.

Subject analysis set title	Olaratumab and Liposomal Doxorubicin
Subject analysis set type	Full analysis

Subject analysis set description:

20 mg/kg of Olaratumab was administered as an IV infusion every 2 weeks (14 days) until there was evidence of PD or development of unacceptable toxicity up to 130 weeks.

40 mg/m² of liposomal doxorubicin was administered according to the manufacturer's instructions every 4 weeks (28 days) until there was evidence of PD or development of unacceptable toxicity.

Subject analysis set title	Olaratumab and Liposomal Doxorubicin
Subject analysis set type	Full analysis

Subject analysis set description:

20 mg/kg of Olaratumab was administered as an IV infusion every 2 weeks (14 days) until there was evidence of PD or development of unacceptable toxicity up to 130 weeks.

40 mg/m² of liposomal doxorubicin was administered according to the manufacturer's instructions every 4 weeks (28 days) until there was evidence of PD or development of unacceptable toxicity.

Primary: Progression-Free Survival (PFS)

End point title	Progression-Free Survival (PFS)

End point description:

PFS is defined as the time from the day of randomization to the first evidence of progression as defined by Response Evaluation Criteria in Solid Tumors version 1.0 (RECIST v1.0) criteria or death from any cause. Participants who died without a reported prior disease progression were considered to have progressed on the day of their death. Participants who did not progress and were subsequently lost to follow-up had their data censored at the day of last tumor assessment.

End point type	Primary

End point timeframe:

Randomization to Progressive Disease (PD) or Date of Death (Up to 35 Months)

End point values	Olaratumab + Liposomal Doxorubicin	Liposomal Doxorubicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62[1]	61[2]		
Units: weeks				
median (confidence interval 90%)	18.1 (8.7 to 27)	17.3 (14.1 to 31.9)		

Notes:

[1] - All randomized participants who received any amount of study drug. Censored participants: 13 and 14.

[2] - All randomized participants who received any amount of study drug. Censored participants: 13 and 14.

Statistical analyses

Statistical analysis title	Progression Free Survival Statistical Analysis

Statistical analysis description:

PFS is defined as the time from the day of randomization to the first evidence of progression as defined by Response Evaluation Criteria in Solid Tumors version 1.0 (RECIST v1.0) criteria or death from any cause. Participants who died without a reported prior disease progression were considered to have progressed on the day of their death. Participants who did not progress and were subsequently lost to follow-up had their data censored at the day of last tumor assessment.

Comparison groups	Olaratumab + Liposomal Doxorubicin v Liposomal Doxorubicin
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8049 [3]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.054
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.751
upper limit	1.478

Notes:

[3] - Stratified by prior platinum treatment, platinum-refractory versus platinum-resistance reaction.

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS is defined as the time from first day of therapy to the date of death from any cause. Participants who were alive at the end of the follow-up period or were lost to follow-up, OS was censored on the last date the participant was known to be alive.

End point type	Secondary

End point timeframe:

First Day of Therapy to Date of Death (Up to 35 Months)

End point values	Olaratumab + Liposomal Doxorubicin	Liposomal Doxorubicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62[4]	61		
Units: weeks				
median (confidence interval 90%)	72.3 (52.4 to 86.7)	70.6 (51.4 to 106.4)		

Notes:

[4] - All randomized participants who received any amount of study drug. Participants censored: 21 and 23

Statistical analyses

Statistical analysis title	Overall Survival Statistical Analysis
Comparison groups	Olaratumab + Liposomal Doxorubicin v Liposomal Doxorubicin
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6346 [5]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.115
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.768
upper limit	1.618

Notes:

[5] - Stratified by prior platinum treatment, platinum-refractory versus platinum-resistance reaction.

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

End point title	Percentage of Participants with Complete Response (CR) or Partial Response (PR) [Objective Response Rate (ORR)]

End point description:

The percentage of participants with a best overall response of confirmed CR or PR defined using RECIST v1.0 criteria. CR is the disappearance of all target and non-target lesions and normalization of cancer antigen-125 (CA-125) levels. PR is defined as having a ≥30% decrease in the sum of the longest diameter (LD) of target lesions taking as reference the baseline sum LD. The percentage of participants with objective response was calculated as: (number of participants whose best overall response of CR or PR/number of participants treated) * 100.

End point type	Secondary

End point timeframe:

Randomization to PD (Up to 35 Months)

End point values	Olaratumab + Liposomal Doxorubicin	Liposomal Doxorubicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62[6]	61		
Units: percentage of participants				
number (confidence interval 90%)	12.9 (6.6 to 22.1)	16.4 (9.2 to 26.2)		

Notes:

[6] - All randomized participants who received any amount of study drug.

Statistical analyses

Statistical analysis title	Objective Response Rate (ORR) Statistical Analysis
Comparison groups	Olaratumab + Liposomal Doxorubicin v Liposomal Doxorubicin
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.619
Method	Fisher exact

Secondary: Median Duration of Response

End point title	Median Duration of Response

End point description:

Duration of response is the interval from the date of initial CR or PR until the first date criteria for PD is met using RECIST v1.0 criteria, or initiation of other (or additional) antitumor therapy is first reported, or death due to any cause. CR is the disappearance of all target and non-target lesions and the normalization of tumor marker levels. PR is a ≥30% decrease in the sum of the LD of target lesions without new lesions and progression of non-target lesions. PD is a ≥20% increase in the sum of the LD of target lesions and/or unequivocal progression of existing non-target lesions and/or detection of 1 or more new lesions. Participants who did not relapse were censored on the day of their last tumor assessment.

End point type	Secondary

End point timeframe:

Date of Initial CR or PR to PD (Up to 35 Months)

End point values	Olaratumab + Liposomal Doxorubicin	Liposomal Doxorubicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8[7]	10[8]		
Units: weeks				
number (confidence interval 90%)	39.1 (26.1 to 56.1)	16.9 (15.3 to 9999)		

Notes:

[7] - All participants who achieved CR or PR. Participants censored: Olaratumab=2, Liposomal Doxorubicin=4

[8] - 9999=N/A. Upper limit of confidence interval (CI) not estimable, did not reach the upper limit of CI

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Adverse Events (AEs) and who died

End point title	Number of Participants with Adverse Events (AEs) and who died

End point description:

Reported are the number of participants with clinically significant events, defined as serious AEs (SAEs) and other non-serious AEs regardless of causality and those who died during treatment and during the 30-day post-dose follow-up. A summary of SAEs and other non-serious AEs regardless of causality is located in the Reported Adverse Events module of this report.

End point type	Secondary

End point timeframe:

Baseline Up to End of Treatment and 30-day Post-dose Follow-up (Up to 35 Months)

End point values	Olaratumab + Liposomal Doxorubicin	Liposomal Doxorubicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62[9]	61		
Units: participants				
number (not applicable)				
SAEs	27	23		
Other Non-SAEs	62	60		
Deaths on treatment or within 30 days of last dose	2	2		

Notes:

[9] - All randomized participants who received any amount of study drug.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Anti-Olaratumab Antibodies

End point title	Percentage of Participants with Anti-Olaratumab Antibodies

End point description:

Participants with Treatment Emergent (TE) anti-olaratumab antibodies were participants with a 4-fold increase (2 dilutions) increase over a positive baseline antibody titer or for a negative baseline titer, a participant with an increase from the baseline to a level of 1:20.

End point type	Secondary

End point timeframe:

Baseline Up to 30-Day Postdose Follow-Up (Up To 35 Months)

End point values	Olaratumab + Liposomal Doxorubicin	Liposomal Doxorubicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57[10]	20[11]		
Units: percentage of participants				
number (not applicable)	1.8	0		

Notes:

[10] - All randomized participants who received at least one dose of study drug and had evaluable data.

[11] - All randomized participants who received at least one dose of study drug and had evaluable data.

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the curve (AUC) of Olaratumab

End point title	Area under the curve (AUC) of Olaratumab

End point description:

End point type	Secondary

End point timeframe:

Prior to and 1 Hour (h) After Olaratumab Infusion in Cycles 1, 2, and 4 and 48 h or 72 h, 144 h, 240 h or 264 h and 336 h Post-dose in Cycles 1 and 4 (28-day Cycles)

End point values	Olaratumab + Liposomal Doxorubicin	Liposomal Doxorubicin	Optional Olaratumab Monotherapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[12]	0[13]	0[14]	
Units: number				
number (not applicable)				

Notes:

[12] - Zero participants were analyzed. Due to technical reasons not related to safety or efficacy.

[13] - Zero participants were analyzed. Due to technical reasons not related to safety or efficacy.

[14] - Zero participants were analyzed. Due to technical reasons not related to safety or efficacy.

Statistical analyses

No statistical analyses for this end point

Secondary: PFS of Participants who Received Olaratumab after Liposomal Doxorubicin monotherapy (Descriptive statistics for safety and efficacy for participants who continue on Olaratumab monotherapy following disease progression on liposomal doxorubicin monotherapy)

End point title	PFS of Participants who Received Olaratumab after Liposomal Doxorubicin monotherapy (Descriptive statistics for safety and efficacy for participants who continue on Olaratumab monotherapy following disease progression on liposomal doxorubicin monotherapy)

End point description:

PFS is defined as the time from start of Olaratumab monotherapy to the first evidence of progression as defined by RECIST v1.0 criteria or death from any cause. Participants who died without a reported prior disease progression were considered to have progressed on the day of their death. Participants who did

not progress and were subsequently lost to follow-up had their data censored at the day of last tumor assessment.

End point type	Secondary

End point timeframe:

From Start of Olaratumab Monotherapy to PD or Date of Death (Up to 20 Weeks)

End point values	Optional Olaratumab Monotherapy			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: weeks				
median (confidence interval 90%)	7.7 (7.1 to 10.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Concentration (Cmax) of Olaratumab

End point title	Maximum Concentration (Cmax) of Olaratumab

End point description:

End point type	Secondary

End point timeframe:

Prior to and 1 h after Olaratumab Infusion in Cycles 1, 2, and 4 and 48 h or 72 h, 144 h, 240 h or 264 h and 336 h Post-dose in Cycles 1 and 4 (28-day Cycles)

End point values	Olaratumab + Liposomal Doxorubicin	Liposomal Doxorubicin	Optional Olaratumab Monotherapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[15]	0[16]	0[17]	
Units: number				
number (not applicable)				

Notes:

[15] - Zero participants were analyzed. Due to technical reasons not related to safety or efficacy.

[16] - Zero participants were analyzed. Due to technical reasons not related to safety or efficacy.

[17] - Zero participants were analyzed. Due to technical reasons not related to safety or efficacy.

Statistical analyses

No statistical analyses for this end point

Secondary: Half-life (t1/2) of Olaratumab

End point title	Half-life (t1/2) of Olaratumab

End point description:

The time it takes to reduce the concentration of Olaratumab in the plasma by 50%.

End point type	Secondary

End point timeframe:

Prior to and 1 h after Olaratumab Infusion in Cycles 1, 2, and 4 and 48 h or 72 h, 144 h, 240 h or 264 h and 336 h Post-dose in Cycles 1 and 4 (28-day Cycles)

End point values	Olaratumab + Liposomal Doxorubicin	Liposomal Doxorubicin	Optional Olaratumab Monotherapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[18]	0[19]	0[20]	
Units: number				
number (not applicable)				

Notes:

[18] - Zero participants were analyzed. Due to technical reasons not related to safety or efficacy.

[19] - Zero participants were analyzed. Due to technical reasons not related to safety or efficacy.

[20] - Zero participants were analyzed. Due to technical reasons not related to safety or efficacy.

Statistical analyses

No statistical analyses for this end point

Secondary: Clearance (CL) of Olaratumab

End point title	Clearance (CL) of Olaratumab

End point description:

CL is the volume of serum cleared of Olaratumab per unit of time after a single dose of Olaratumab

End point type	Secondary

End point timeframe:

Prior to and 1 h after Olaratumab Infusion in Cycles 1, 2, and 4 and 48 h or 72 h, 144 h, 240 h or 264 h and 336 h Post-dose in Cycles 1 and 4 (28-day Cycles)

End point values	Olaratumab + Liposomal Doxorubicin	Liposomal Doxorubicin	Optional Olaratumab Monotherapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[21]	0[22]	0[23]	
Units: number				
number (not applicable)				

Notes:

[21] - Zero participants were analyzed. Due to technical reasons not related to safety or efficacy.

[22] - Zero participants were analyzed. Due to technical reasons not related to safety or efficacy.

[23] - Zero participants were analyzed. Due to technical reasons not related to safety or efficacy.

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Volume of distribution (Vss) of Olaratumab

End point title	Apparent Volume of distribution (Vss) of Olaratumab

End point description:

Vss is an estimate of drug distribution independent of the elimination process and is proportional to the amount of drug in the body versus the drug plasma concentration at steady-state.

End point type	Secondary

End point timeframe:

Prior to and 1 h after Olaratumab Infusion in Cycles 1, 2, and 4 and 48 h or 72 h, 144 h, 240 h or 264 h and 336 h Post-dose in Cycles 1 and 4 (28-day Cycles)

End point values	Olaratumab + Liposomal Doxorubicin	Liposomal Doxorubicin	Optional Olaratumab Monotherapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[24]	0[25]	0[26]	
Units: number				
number (not applicable)				

Notes:

[24] - Zero participants were analyzed. Due to technical reasons not related to safety or efficacy.

[25] - Zero participants were analyzed. Due to technical reasons not related to safety or efficacy.

[26] - Zero participants were analyzed. Due to technical reasons not related to safety or efficacy.

Statistical analyses

No statistical analyses for this end point

Secondary: PFS for Participants who had Tissue Samples for Platelet Derived Growth Factor Receptor Alpha (PDGFRα) Expression Determined by Immunohistochemistry (IHC) (Association between PDGFRα tumor expression and PFS)

End point title	PFS for Participants who had Tissue Samples for Platelet Derived Growth Factor Receptor Alpha (PDGFRα) Expression Determined by Immunohistochemistry (IHC) (Association between PDGFRα tumor expression and PFS)

End point description:

PFS is defined as the time from the day of randomization to the first evidence of progression as defined by RECIST v1.0 criteria or death from any cause. Participants who died without a reported prior disease progression were considered to have progressed on the day of their death. Participants who did not progress and were subsequently lost to follow-up had their data censored at the day of last tumor assessment. PDGFRα protein expression at baseline in tumor cells is determined by IHC using H-Scores and a cut point of 0. Participants were considered to have a high relative expression when H-Score is >0 and a low relative expression when H-Score=0. H-Score was calculated by summing the percentage of cell staining at each intensity multiplied by the weighted intensity of staining. Staining intensity: 0 (no staining), 1+ (weak staining), 2+ (medium staining), 3+ (strongest staining). H-Scores could range from 0-300.

End point type	Secondary

End point timeframe:

Randomization to PD or Date of Death (Up to 130 Weeks)

End point values	Olaratumab + Liposomal Doxorubicin	Liposomal Doxorubicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54[27]	47		
Units: weeks				
median (confidence interval 95%)				
High Expression (n=41, 36)	21 (8.7 to 34.1)	17.3 (12.3 to 33.9)		
Low Expression (n=13,11)	32.7 (7.6 to 41.3)	24 (8.1 to 36.1)		

Notes:

[27] - All participants who had evaluable PDGFRα results.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Entire Study	
Adverse event reporting additional description:	
I5B-IE-JGDA	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups	
Reporting group title	Olaratumab + Liposomal Doxorubicin
Reporting group description: -	
Reporting group title	Optional Olaratumab Monotherapy
Reporting group description: -	
Reporting group title	Liposomal Doxorubicin
Reporting group description: -	

Serious adverse events	Olaratumab + Liposomal Doxorubicin	Optional Olaratumab Monotherapy	Liposomal Doxorubicin
Total subjects affected by serious adverse events			
subjects affected / exposed	27 / 62 (43.55%)	14 / 28 (50.00%)	23 / 61 (37.70%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
venous thrombosis			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	0 / 62 (0.00%)	0 / 28 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
chills			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	1 / 62 (1.61%)	0 / 28 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
disease progression			
alternative dictionary used: MedDRA 14.1			

subjects affected / exposed	0 / 62 (0.00%)	0 / 28 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
extravasation			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	0 / 62 (0.00%)	0 / 28 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
infusion site erythema			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	0 / 62 (0.00%)	0 / 28 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
mucosal inflammation			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	0 / 62 (0.00%)	1 / 28 (3.57%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pyrexia			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	2 / 62 (3.23%)	2 / 28 (7.14%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
hypersensitivity			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	0 / 62 (0.00%)	1 / 28 (3.57%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
dyspnoea			
alternative dictionary used: MedDRA 14.1			

subjects affected / exposed	0 / 62 (0.00%)	1 / 28 (3.57%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
interstitial lung disease			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	0 / 62 (0.00%)	0 / 28 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pleural effusion			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	0 / 62 (0.00%)	1 / 28 (3.57%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pulmonary embolism			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	2 / 62 (3.23%)	0 / 28 (0.00%)	4 / 61 (6.56%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Psychiatric disorders			
bradyphrenia			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	1 / 62 (1.61%)	0 / 28 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
femur fracture			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	0 / 62 (0.00%)	0 / 28 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
incorrect drug administration duration			
alternative dictionary used: MedDRA 14.1			

subjects affected / exposed	1 / 62 (1.61%)	0 / 28 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
medication error			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	1 / 62 (1.61%)	1 / 28 (3.57%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
pyloric stenosis			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	0 / 62 (0.00%)	0 / 28 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
cardiac failure congestive			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	0 / 62 (0.00%)	0 / 28 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
coronary artery stenosis			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	1 / 62 (1.61%)	0 / 28 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	0 / 62 (0.00%)	0 / 28 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
haemorrhage intracranial			
alternative dictionary used: MedDRA 14.1			

subjects affected / exposed	1 / 62 (1.61%)	0 / 28 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
syncope			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	1 / 62 (1.61%)	0 / 28 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	1 / 62 (1.61%)	1 / 28 (3.57%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
abdominal discomfort			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	1 / 62 (1.61%)	0 / 28 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
abdominal distension			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	2 / 62 (3.23%)	0 / 28 (0.00%)	2 / 61 (3.28%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
abdominal pain			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	0 / 62 (0.00%)	1 / 28 (3.57%)	3 / 61 (4.92%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ascites			
alternative dictionary used: MedDRA 14.1			

subjects affected / exposed	0 / 62 (0.00%)	0 / 28 (0.00%)	3 / 61 (4.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
constipation			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	1 / 62 (1.61%)	0 / 28 (0.00%)	2 / 61 (3.28%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
diarrhoea			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	1 / 62 (1.61%)	0 / 28 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	3 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
duodenal stenosis			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	0 / 62 (0.00%)	1 / 28 (3.57%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
gastrointestinal obstruction			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	0 / 62 (0.00%)	1 / 28 (3.57%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ileus			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	0 / 62 (0.00%)	0 / 28 (0.00%)	2 / 61 (3.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
intestinal obstruction			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	3 / 62 (4.84%)	1 / 28 (3.57%)	2 / 61 (3.28%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

nausea			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	1 / 62 (1.61%)	2 / 28 (7.14%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
proctitis			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	1 / 62 (1.61%)	0 / 28 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
rectal haemorrhage			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	0 / 62 (0.00%)	1 / 28 (3.57%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
small intestinal obstruction			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	1 / 62 (1.61%)	0 / 28 (0.00%)	4 / 61 (6.56%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
vomiting			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	3 / 62 (4.84%)	2 / 28 (7.14%)	3 / 61 (4.92%)
occurrences causally related to treatment / all	1 / 3	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
bile duct obstruction			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	0 / 62 (0.00%)	1 / 28 (3.57%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
hydronephrosis			
alternative dictionary used: MedDRA 14.1			

subjects affected / exposed	1 / 62 (1.61%)	1 / 28 (3.57%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
renal failure			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	0 / 62 (0.00%)	0 / 28 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
renal failure acute			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	1 / 62 (1.61%)	0 / 28 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
flank pain			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	0 / 62 (0.00%)	1 / 28 (3.57%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
bacillus infection			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	0 / 62 (0.00%)	0 / 28 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cellulitis			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	0 / 62 (0.00%)	0 / 28 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
device related infection			
alternative dictionary used: MedDRA 14.1			

subjects affected / exposed	2 / 62 (3.23%)	0 / 28 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
febrile infection			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	0 / 62 (0.00%)	0 / 28 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
gastroenteritis			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	0 / 62 (0.00%)	0 / 28 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
infection			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	2 / 62 (3.23%)	0 / 28 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pharyngitis			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	0 / 62 (0.00%)	1 / 28 (3.57%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumonia			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	1 / 62 (1.61%)	0 / 28 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
urinary tract infection			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	0 / 62 (0.00%)	0 / 28 (0.00%)	2 / 61 (3.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

urinary tract infection fungal			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	0 / 62 (0.00%)	0 / 28 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
urosepsis			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	1 / 62 (1.61%)	0 / 28 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
viral infection			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	1 / 62 (1.61%)	0 / 28 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	1 / 62 (1.61%)	0 / 28 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
dehydration			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	3 / 62 (4.84%)	0 / 28 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Olaratumab + Liposomal Doxorubicin	Optional Olaratumab Monotherapy	Liposomal Doxorubicin
Total subjects affected by non-serious adverse events			
subjects affected / exposed	62 / 62 (100.00%)	27 / 28 (96.43%)	60 / 61 (98.36%)
Vascular disorders			

flushing			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	4 / 62 (6.45%)	0 / 28 (0.00%)	1 / 61 (1.64%)
occurrences (all)	4	0	1
hypertension			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	4 / 62 (6.45%)	1 / 28 (3.57%)	3 / 61 (4.92%)
occurrences (all)	4	1	3
hypotension			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	4 / 62 (6.45%)	0 / 28 (0.00%)	1 / 61 (1.64%)
occurrences (all)	5	0	1
General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	8 / 62 (12.90%)	4 / 28 (14.29%)	11 / 61 (18.03%)
occurrences (all)	11	6	21
early satiety			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	3 / 62 (4.84%)	0 / 28 (0.00%)	4 / 61 (6.56%)
occurrences (all)	3	0	4
fatigue			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	33 / 62 (53.23%)	5 / 28 (17.86%)	27 / 61 (44.26%)
occurrences (all)	64	6	50
mucosal inflammation			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	12 / 62 (19.35%)	2 / 28 (7.14%)	15 / 61 (24.59%)
occurrences (all)	19	3	38
oedema peripheral			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	10 / 62 (16.13%)	3 / 28 (10.71%)	12 / 61 (19.67%)
occurrences (all)	13	3	16
pyrexia			
alternative dictionary used:			

MedDRA 14.1			
subjects affected / exposed	8 / 62 (12.90%)	3 / 28 (10.71%)	7 / 61 (11.48%)
occurrences (all)	15	3	7
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	10 / 62 (16.13%)	2 / 28 (7.14%)	7 / 61 (11.48%)
occurrences (all)	10	2	7
dyspnoea			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	10 / 62 (16.13%)	4 / 28 (14.29%)	10 / 61 (16.39%)
occurrences (all)	11	4	12
oropharyngeal pain			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	5 / 62 (8.06%)	0 / 28 (0.00%)	3 / 61 (4.92%)
occurrences (all)	5	0	4
pleural effusion			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	6 / 62 (9.68%)	2 / 28 (7.14%)	4 / 61 (6.56%)
occurrences (all)	11	3	4
Psychiatric disorders			
anxiety			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	7 / 62 (11.29%)	0 / 28 (0.00%)	6 / 61 (9.84%)
occurrences (all)	7	0	6
insomnia			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	5 / 62 (8.06%)	1 / 28 (3.57%)	3 / 61 (4.92%)
occurrences (all)	5	1	3
Investigations			
haemoglobin decreased			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	7 / 62 (11.29%)	2 / 28 (7.14%)	4 / 61 (6.56%)
occurrences (all)	8	3	4
neutrophil count decreased			

alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	3 / 62 (4.84%)	0 / 28 (0.00%)	5 / 61 (8.20%)
occurrences (all)	6	0	5
weight decreased			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	9 / 62 (14.52%)	1 / 28 (3.57%)	4 / 61 (6.56%)
occurrences (all)	10	1	4
white blood cell count decreased			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	6 / 62 (9.68%)	0 / 28 (0.00%)	3 / 61 (4.92%)
occurrences (all)	27	0	3
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	10 / 62 (16.13%)	1 / 28 (3.57%)	10 / 61 (16.39%)
occurrences (all)	12	1	13
dysgeusia			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	10 / 62 (16.13%)	0 / 28 (0.00%)	3 / 61 (4.92%)
occurrences (all)	12	0	6
headache			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	12 / 62 (19.35%)	6 / 28 (21.43%)	7 / 61 (11.48%)
occurrences (all)	18	7	8
lethargy			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	6 / 62 (9.68%)	0 / 28 (0.00%)	4 / 61 (6.56%)
occurrences (all)	10	0	6
neuropathy peripheral			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	5 / 62 (8.06%)	0 / 28 (0.00%)	2 / 61 (3.28%)
occurrences (all)	6	0	4
paraesthesia			
alternative dictionary used: MedDRA 14.1			

subjects affected / exposed	3 / 62 (4.84%)	0 / 28 (0.00%)	6 / 61 (9.84%)
occurrences (all)	4	0	7
tremor			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	4 / 62 (6.45%)	0 / 28 (0.00%)	0 / 61 (0.00%)
occurrences (all)	4	0	0
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	10 / 62 (16.13%)	6 / 28 (21.43%)	13 / 61 (21.31%)
occurrences (all)	21	8	23
leukopenia			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	6 / 62 (9.68%)	0 / 28 (0.00%)	2 / 61 (3.28%)
occurrences (all)	10	0	2
lymphadenopathy			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	4 / 62 (6.45%)	0 / 28 (0.00%)	0 / 61 (0.00%)
occurrences (all)	5	0	0
neutropenia			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	16 / 62 (25.81%)	2 / 28 (7.14%)	8 / 61 (13.11%)
occurrences (all)	67	3	23
Gastrointestinal disorders			
abdominal discomfort			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	1 / 62 (1.61%)	2 / 28 (7.14%)	3 / 61 (4.92%)
occurrences (all)	1	2	3
abdominal distension			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	14 / 62 (22.58%)	5 / 28 (17.86%)	6 / 61 (9.84%)
occurrences (all)	18	5	8
abdominal pain			
alternative dictionary used: MedDRA 14.1			

subjects affected / exposed	15 / 62 (24.19%)	3 / 28 (10.71%)	25 / 61 (40.98%)
occurrences (all)	22	3	35
abdominal pain lower			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	4 / 62 (6.45%)	2 / 28 (7.14%)	5 / 61 (8.20%)
occurrences (all)	4	3	6
abdominal pain upper			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	10 / 62 (16.13%)	2 / 28 (7.14%)	7 / 61 (11.48%)
occurrences (all)	11	3	8
ascites			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	12 / 62 (19.35%)	5 / 28 (17.86%)	6 / 61 (9.84%)
occurrences (all)	17	6	9
constipation			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	32 / 62 (51.61%)	7 / 28 (25.00%)	24 / 61 (39.34%)
occurrences (all)	40	8	33
diarrhoea			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	19 / 62 (30.65%)	5 / 28 (17.86%)	13 / 61 (21.31%)
occurrences (all)	28	5	16
dry mouth			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	5 / 62 (8.06%)	0 / 28 (0.00%)	1 / 61 (1.64%)
occurrences (all)	5	0	1
dyspepsia			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	8 / 62 (12.90%)	7 / 28 (25.00%)	7 / 61 (11.48%)
occurrences (all)	14	7	7
dysphagia			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	4 / 62 (6.45%)	0 / 28 (0.00%)	3 / 61 (4.92%)
occurrences (all)	5	0	5

flatulence			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	2 / 62 (3.23%)	0 / 28 (0.00%)	4 / 61 (6.56%)
occurrences (all)	2	0	5
gastrooesophageal reflux disease			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	7 / 62 (11.29%)	1 / 28 (3.57%)	6 / 61 (9.84%)
occurrences (all)	7	1	7
nausea			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	35 / 62 (56.45%)	13 / 28 (46.43%)	39 / 61 (63.93%)
occurrences (all)	61	16	61
odynophagia			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	1 / 62 (1.61%)	0 / 28 (0.00%)	4 / 61 (6.56%)
occurrences (all)	2	0	4
stomatitis			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	23 / 62 (37.10%)	2 / 28 (7.14%)	16 / 61 (26.23%)
occurrences (all)	40	2	34
vomiting			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	21 / 62 (33.87%)	10 / 28 (35.71%)	18 / 61 (29.51%)
occurrences (all)	41	12	33
Skin and subcutaneous tissue disorders			
alopecia			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	10 / 62 (16.13%)	1 / 28 (3.57%)	9 / 61 (14.75%)
occurrences (all)	11	1	10
blister			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	7 / 62 (11.29%)	1 / 28 (3.57%)	7 / 61 (11.48%)
occurrences (all)	11	1	11
dry skin			
alternative dictionary used: MedDRA 14.1			

subjects affected / exposed	8 / 62 (12.90%)	0 / 28 (0.00%)	10 / 61 (16.39%)
occurrences (all)	11	0	11
erythema			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	7 / 62 (11.29%)	0 / 28 (0.00%)	8 / 61 (13.11%)
occurrences (all)	7	0	10
night sweats			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	0 / 62 (0.00%)	2 / 28 (7.14%)	0 / 61 (0.00%)
occurrences (all)	0	2	0
palmar-plantar erythrodysaesthesia syndrome			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	21 / 62 (33.87%)	1 / 28 (3.57%)	27 / 61 (44.26%)
occurrences (all)	54	2	60
pruritus			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	3 / 62 (4.84%)	1 / 28 (3.57%)	5 / 61 (8.20%)
occurrences (all)	3	1	5
rash			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	24 / 62 (38.71%)	4 / 28 (14.29%)	14 / 61 (22.95%)
occurrences (all)	37	5	34
skin discolouration			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	4 / 62 (6.45%)	0 / 28 (0.00%)	2 / 61 (3.28%)
occurrences (all)	4	0	2
skin hyperpigmentation			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	3 / 62 (4.84%)	0 / 28 (0.00%)	6 / 61 (9.84%)
occurrences (all)	4	0	11
Renal and urinary disorders			
hydronephrosis			
alternative dictionary used: MedDRA 14.1			

subjects affected / exposed	1 / 62 (1.61%)	2 / 28 (7.14%)	1 / 61 (1.64%)
occurrences (all)	1	3	1
pollakiuria			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	4 / 62 (6.45%)	0 / 28 (0.00%)	2 / 61 (3.28%)
occurrences (all)	5	0	2
proteinuria			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	7 / 62 (11.29%)	1 / 28 (3.57%)	2 / 61 (3.28%)
occurrences (all)	10	1	2
renal failure			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	0 / 62 (0.00%)	2 / 28 (7.14%)	0 / 61 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	11 / 62 (17.74%)	1 / 28 (3.57%)	7 / 61 (11.48%)
occurrences (all)	13	1	8
back pain			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	16 / 62 (25.81%)	5 / 28 (17.86%)	9 / 61 (14.75%)
occurrences (all)	18	6	12
muscle spasms			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	7 / 62 (11.29%)	3 / 28 (10.71%)	3 / 61 (4.92%)
occurrences (all)	14	3	3
musculoskeletal pain			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	4 / 62 (6.45%)	1 / 28 (3.57%)	0 / 61 (0.00%)
occurrences (all)	4	1	0
pain in extremity			
alternative dictionary used: MedDRA 14.1			

subjects affected / exposed	4 / 62 (6.45%)	1 / 28 (3.57%)	9 / 61 (14.75%)
occurrences (all)	5	2	9
Infections and infestations			
candidiasis			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	4 / 62 (6.45%)	0 / 28 (0.00%)	0 / 61 (0.00%)
occurrences (all)	4	0	0
oral candidiasis			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	2 / 62 (3.23%)	2 / 28 (7.14%)	2 / 61 (3.28%)
occurrences (all)	3	2	3
upper respiratory tract infection			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	3 / 62 (4.84%)	2 / 28 (7.14%)	4 / 61 (6.56%)
occurrences (all)	4	2	5
urinary tract infection			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	15 / 62 (24.19%)	3 / 28 (10.71%)	3 / 61 (4.92%)
occurrences (all)	23	3	5
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	15 / 62 (24.19%)	10 / 28 (35.71%)	13 / 61 (21.31%)
occurrences (all)	31	10	19
dehydration			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	7 / 62 (11.29%)	1 / 28 (3.57%)	2 / 61 (3.28%)
occurrences (all)	7	1	2
hyperglycaemia			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	0 / 62 (0.00%)	0 / 28 (0.00%)	4 / 61 (6.56%)
occurrences (all)	0	0	5
hypokalaemia			
alternative dictionary used: MedDRA 14.1			

subjects affected / exposed	5 / 62 (8.06%)	4 / 28 (14.29%)	7 / 61 (11.48%)
occurrences (all)	8	5	8
hypomagnesaemia			
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	8 / 62 (12.90%)	2 / 28 (7.14%)	6 / 61 (9.84%)
occurrences (all)	15	3	8

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 March 2010	Protocol Version 2.0 dated 10-Mar-2010 Changes from Version 1.2 • This protocol is being amended primarily to incorporate new procedures in blood sampling for pharmacodynamic analyses. Additional changes to study procedures have been made and language regarding existing study procedures has been modified for the sake of clarity.
13 April 2010	Protocol Version 2.1 dated 13-Apr-2010 • This administrative amendment, Version 2.1, was instituted to make clear that all study procedures, with the exception of those performed every 8 weeks (ie, imaging studies/tumor assessments), are performed relative to treatment cycles, and not at fixed intervals. The actual (not planned) administration of each liposomal doxorubicin infusion will define Day 1 of each 28-day treatment cycle. Therefore, treatment delays, for whatever reason, will also cause an equivalent delay in all other study procedures (with the exception of imaging studies/tumor assessments). Language throughout Section 7, Study Activities, was clarified accordingly, and an additional sentence was added to Section 4, Investigational Plan, to provide a definition of "treatment cycle."

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported