



Clinical trial results:

A Randomized Phase 2 Study of Human Anti-PDGFR Monoclonal Antibody IMC-3G3 Plus Mitoxantrone Plus Prednisone or Mitoxantrone Plus Prednisone in Metastatic Castration-Refractory Prostate Cancer Following Disease Progression or Intolerance on Docetaxel-based Chemotherapy

Summary

EudraCT number	2009-018015-11
Trial protocol	DE BE ES CZ IT HU
Global end of trial date	01 October 2013

Results information

Result version number	v1
This version publication date	04 December 2016
First version publication date	04 December 2016

Trial information

Trial identification

Sponsor protocol code	13938
-----------------------	-------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01204710
WHO universal trial number (UTN)	-
Other trial identifiers	Trial alias: I5B-IE-JGDD, Trial number: 13938

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, Eli Lilly and Company, 1 877-CTLilly,
Scientific contact	Available Mon-Fri 9 am - 5 pm, 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	01 October 2013
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	01 October 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This is a study evaluating the safety and efficacy of the monoclonal antibody olaratumab plus mitoxantrone plus prednisone compared to mitoxantrone plus prednisone in metastatic castration-refractory prostate cancer following disease progression or intolerance on docetaxel-based chemotherapy.

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	06 October 2010
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	Hungary: 16
Country: Number of subjects enrolled	Czech Republic: 7
Country: Number of subjects enrolled	Spain: 29
Country: Number of subjects enrolled	Poland: 17
Country: Number of subjects enrolled	Belgium: 6
Country: Number of subjects enrolled	Germany: 31
Country: Number of subjects enrolled	Italy: 17
Worldwide total number of subjects	123
EEA total number of subjects	123

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)	36
From 65 to 84 years	87
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A participant was considered to have completed the study if he or she experienced progressive disease (PD) or had died.

Period 1

Period 1 title	Randomization Treatment
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Olaratumab (IMC-3G3) + Mitoxantrone

Arm description:

15 milligrams per kilogram (mg/kg) olaratumab was administered intravenously (IV) on Days 1 and 8 of each 21-day cycle, followed by 12 milligrams per square meter (mg/m²) mitoxantrone IV on Day 1 of each 21-day cycle with 5 milligrams (mg) prednisone orally (PO) twice daily (BID) on each day. Mitoxantrone was administered for up to 12 cycles (total cumulative dose of mitoxantrone was restricted to ≤ 144 mg/m²).

After 12 cycles, participants continued to receive 15 mg/kg olaratumab IV on Days 1 and 8 of each 21-day cycle with 5 mg prednisone PO BID on each day until withdrawal criteria were met.

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

Dosage and administration details:

15 milligrams per kilogram (mg/kg) olaratumab was administered intravenously (IV) on Days 1 and 8 of each 21-day cycle, followed by 12 milligrams per square meter (mg/m²) mitoxantrone IV on Day 1 of each 21-day cycle with 5 milligrams (mg) prednisone orally (PO) twice daily (BID) on each day.

Mitoxantrone was administered for up to 12 cycles (total cumulative dose of mitoxantrone was restricted to ≤ 144 mg/m²).

After 12 cycles, participants continued to receive 15 mg/kg olaratumab IV on Days 1 and 8 of each 21-day cycle with 5 mg prednisone PO BID on each day until withdrawal criteria were met.

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

Dosage and administration details:

Mitoxantrone was administered for up to 12 cycles (total cumulative dose of mitoxantrone was restricted to ≤ 144 mg/m²).

Arm title	Mitoxantrone
------------------	--------------

Arm description:

12 mg/m² mitoxantrone was administered IV on Day 1 of each 21-day cycle with 5 mg prednisone PO BID on each day.

Mitoxantrone was administered for up to 12 cycles (total cumulative dose of mitoxantrone is restricted

to ≤ 144 mg/m²).

PO BID on each day. Participants received treatment until withdrawal criteria were met.

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

Dosage and administration details:

12 mg/m² mitoxantrone was administered IV on Day 1 of each 21-day cycle with 5 mg prednisone PO BID on each day.

Mitoxantrone was administered for up to 12 cycles (total cumulative dose of mitoxantrone is restricted to ≤ 144 mg/m²).

Number of subjects in period 1	Olaratumab (IMC-3G3) + Mitoxantrone	Mitoxantrone
Started	63	60
Received ≥ 1 dose of study drug	62	59
Completed	49	47
Not completed	14	13
Consent withdrawn by subject	6	5
Physician decision	3	2
Moved and Followed for Survival	-	1
Adverse event, non-fatal	4	2
Sponsor Decision	-	1
Lost to follow-up	1	-
Worsening of General condition	-	1
Entry criteria not met	-	1

Period 2

Period 2 title	Optional 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: Participants who experienced PD had the option to receive olaratumab monotherapy treatment. 15 mg/kg olaratumab was administered IV on Days 1 and 8 of each 21-day cycle with 5 mg prednisone PO BID on each day. Participants received treatment until withdrawal criteria were met. These participants are a subset of the control arm.	
Arm type	Experimental
Investigational medicinal product name	Olaratumab
Investigational medicinal product code	
Other name	IMC-3G3, LY3012207
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

15 milligrams per kilogram (mg/kg) olaratumab was administered intravenously (IV) on Days 1 and 8 of each 21-day cycle

Number of subjects in period 2^[1]	Optional Olaratumab Monotherapy
Started	19
Completed	16
Not completed	3
Physician decision	1
Consent withdrawn by subject	1
Olaratumab Intolerance	1

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: Olaratumab follow-on treatment was optional for participants in mitoxantrone group only who had PD.

Among 43 participants who experienced PD, 19 received olaratumab follow-on treatment.

Baseline characteristics

Reporting groups

Reporting group title	Olaratumab (IMC-3G3) + Mitoxantrone
-----------------------	-------------------------------------

Reporting group description:

15 milligrams per kilogram (mg/kg) olaratumab was administered intravenously (IV) on Days 1 and 8 of each 21-day cycle, followed by 12 milligrams per square meter (mg/m²) mitoxantrone IV on Day 1 of each 21-day cycle with 5 milligrams (mg) prednisone orally (PO) twice daily (BID) on each day.

Mitoxantrone was administered for up to 12 cycles (total cumulative dose of mitoxantrone was restricted to ≤144 mg/m²).

After 12 cycles, participants continued to receive 15 mg/kg olaratumab IV on Days 1 and 8 of each 21-day cycle with 5 mg prednisone PO BID on each day until withdrawal criteria were met.

Reporting group title	Mitoxantrone
-----------------------	--------------

Reporting group description:

12 mg/m² mitoxantrone was administered IV on Day 1 of each 21-day cycle with 5 mg prednisone PO BID on each day.

Mitoxantrone was administered for up to 12 cycles (total cumulative dose of mitoxantrone is restricted to ≤144 mg/m²).

PO BID on each day. Participants received treatment until withdrawal criteria were met.

Reporting group values	Olaratumab (IMC-3G3) + Mitoxantrone	Mitoxantrone	Total
Number of subjects	63	60	123
Age Categorical Units: participants			
≤18 years	0	0	0
Between 18 and 65 years	20	16	36
≥65 years	43	44	87
Gender, Male/Female Units: participants			
Female	0	0	0
Male	63	60	123
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	3	5
Not Hispanic or Latino	61	57	118
Unknown or Not Reported	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	63	59	122
More than one race	0	1	1
Unknown or Not Reported	0	0	0
Region of Enrollment Units: Subjects			
Hungary	6	10	16

Czech Republic	5	2	7
Spain	17	12	29
Poland	11	6	17
Belgium	3	3	6
Germany	15	16	31
Italy	6	11	17

End points

End points reporting groups

Reporting group title	Olaratumab (IMC-3G3) + Mitoxantrone
-----------------------	-------------------------------------

Reporting group description:

15 milligrams per kilogram (mg/kg) olaratumab was administered intravenously (IV) on Days 1 and 8 of each 21-day cycle, followed by 12 milligrams per square meter (mg/m²) mitoxantrone IV on Day 1 of each 21-day cycle with 5 milligrams (mg) prednisone orally (PO) twice daily (BID) on each day.

Mitoxantrone was administered for up to 12 cycles (total cumulative dose of mitoxantrone was restricted to ≤ 144 mg/m²).

After 12 cycles, participants continued to receive 15 mg/kg olaratumab IV on Days 1 and 8 of each 21-day cycle with 5 mg prednisone PO BID on each day until withdrawal criteria were met.

Reporting group title	Mitoxantrone
-----------------------	--------------

Reporting group description:

12 mg/m² mitoxantrone was administered IV on Day 1 of each 21-day cycle with 5 mg prednisone PO BID on each day.

Mitoxantrone was administered for up to 12 cycles (total cumulative dose of mitoxantrone is restricted to ≤ 144 mg/m²).

PO BID on each day. Participants received treatment until withdrawal criteria were met.

Reporting group title	Optional Olaratumab Monotherapy
-----------------------	---------------------------------

Reporting group description:

Participants who experienced PD had the option to receive olaratumab monotherapy treatment. 15 mg/kg olaratumab was administered IV on Days 1 and 8 of each 21-day cycle with 5 mg prednisone PO BID on each day. Participants received treatment until withdrawal criteria were met. These participants are a subset of the control arm.

Subject analysis set title	Optional Olaratumab Monotherapy
----------------------------	---------------------------------

Subject analysis set type	Per protocol
---------------------------	--------------

Subject analysis set description:

Participants who experienced PD had the option to receive olaratumab monotherapy treatment. 15 mg/kg olaratumab was administered IV on Days 1 and 8 of each 21-day cycle with 5 mg prednisone

Subject analysis set title	PFS Olaratumab + Mitoxantrone + Mitoxantrone (LE)
----------------------------	---

Subject analysis set type	Sub-group analysis
---------------------------	--------------------

Subject analysis set description:

All randomized participants who had CTC counts at baseline in the Olaratumab + Mitoxantrone arm and the Mitoxantrone arm. Low expression (LE) of CTC was defined as having CTC counts < 5 cells/7.5 mL. PFS is measured from

randomization to the earliest date of the following events: PD according to RECIST criteria v. 1.1, is a $\geq 20\%$ increase in the sum diameter of the target lesions taking as reference the smallest sum on study and an absolute increase in the sum diameter of ≥ 5 mm, the appearance of 1 or more new lesions and/or unequivocal progression of existing nontarget lesions, unequivocal evidence of progression by bone scan, clinical progression or death from any cause. For participants who had no documented PD or death or had started new anti-cancer therapy, PFS was censored at their last tumor assessment.

Subject analysis set title	PFS Olaratumab + Mitoxantrone and Mitoxantrone (HE)
----------------------------	---

Subject analysis set type	Sub-group analysis
---------------------------	--------------------

Subject analysis set description:

All randomized participants who had CTC counts at baseline in the Olaratumab + Mitoxantrone arm and the Mitoxantrone arm. High expression (HE) of CTC was defined as having CTC counts ≥ 5 cells/7.5 milliliter (mL). PFS is

measured from randomization to the earliest date of the following events: PD according to RECIST criteria v. 1.1, is a $\geq 20\%$ increase in the sum diameter of the target lesions taking as reference the smallest sum on study and an absolute increase in the sum diameter of ≥ 5 mm, the appearance of 1 or more new lesions and/or unequivocal progression of existing nontarget lesions, unequivocal evidence of progression by bone scan, clinical progression or death from any cause. For participants who had no documented PD or death or had started new anti-cancer therapy, PFS was censored at their last tumor assessment.

Subject analysis set title	OS Olaratumab + Mitoxantrone + Mitoxantrone (LE)
----------------------------	--

Subject analysis set type	Sub-group analysis
---------------------------	--------------------

Subject analysis set description:

All randomized participants who had CTC counts at baseline in the Olaratumab + Mitoxantrone arm and the Mitoxantrone arm. LE of CTC was defined as having CTC counts <5 cells/7.5 mL.

Subject analysis set title	OS Olaratumab + Mitoxantrone and Mitoxantrone (HE)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All randomized participants who had CTC counts at baseline in the Olaratumab + Mitoxantrone arm and the Mitoxantrone arm. HE of CTC was defined as having CTC counts ≥ 5 cells/7.5 mL

Primary: Progression-Free survival (PFS)

End point title	Progression-Free survival (PFS)
-----------------	---------------------------------

End point description:

PFS is measured from randomization to the earliest date of the following events: PD according to Response Evaluation Criteria In Solid Tumors (RECIST) criteria version (v) 1.1, is a $\geq 20\%$ increase in the sum of diameter of the target lesions taking as reference the smallest sum on study and an absolute increase in the sum diameter of ≥ 5 millimeter (mm), the appearance of 1 or more new lesions and/or unequivocal progression of existing nontarget lesions, unequivocal evidence of progression by bone scan, clinical progression or death from any cause. For participants who had no documented PD or death or had started new anti-cancer therapy or were lost to follow-up, PFS was censored at their last tumor assessment.

End point type	Primary
----------------	---------

End point timeframe:

Randomization to Measured PD or Death Due to Any Cause Up to 23 Months

End point values	Olaratumab (IMC-3G3) + Mitoxantrone	Mitoxantrone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62 ^[1]	59 ^[2]		
Units: months				
median (confidence interval 95%)	2.3 (2.2 to 2.8)	2.4 (2.2 to 3.8)		

Notes:

[1] - All randomized participants who received ≥ 1 dose of study drug.

[2] - All randomized participants who received ≥ 1 dose of study drug.

Statistical analyses

Statistical analysis title	Statistical Analysis for Progression-Free Survival
Comparison groups	Olaratumab (IMC-3G3) + Mitoxantrone v Mitoxantrone
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2201 ^[3]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.9

Notes:

[3] - Analysis was stratified by the randomization stratification factor: best overall response to prior docetaxel-based chemotherapy.

Secondary: Overall survival (OS)

End point title	Overall survival (OS)
-----------------	-----------------------

End point description:

OS was defined as the time from the date of randomization to the date of death from any cause. If the participants were alive at the end of the follow-up period or were lost to follow-up, OS time was censored on the last date the participant was known to be alive.

End point type	Secondary
----------------	-----------

End point timeframe:

Randomization to Death Due to Any Cause Up to 36 Months

End point values	Olaratumab (IMC-3G3) + Mitoxantrone	Mitoxantrone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62 ^[4]	59 ^[5]		
Units: months				
median (confidence interval 95%)	14.2 (12.2 to 16)	12.8 (8.1 to 16.4)		

Notes:

[4] - All randomized participants who received ≥ 1 dose of study drug.

[5] - All randomized participants who received ≥ 1 dose of study drug.

Statistical analyses

Statistical analysis title	Statistical Analysis for Overall Survival
Comparison groups	Mitoxantrone v Olaratumab (IMC-3G3) + Mitoxantrone
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7291 ^[6]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	1.61

Notes:

[6] - Analysis was stratified by the randomization stratification factor: best overall response to prior docetaxel-based chemotherapy.

Secondary: Percentage of participants who achieved a best overall response of complete response (CR) or partial response (PR) [Objective Response Rate (ORR)]

End point title	Percentage of participants who achieved a best overall response of complete response (CR) or partial response (PR) [Objective Response Rate (ORR)]
-----------------	--

End point description:

Best response is categorized using the RECIST v1.1 guidelines. CR is the disappearance of all non-nodal target lesions, with the short axes of any target lymph nodes reduced to <10 mm. PR is a $\geq 30\%$ decrease in the sum of the diameters of target lesions (including the short axes of any target lymph nodes), taking as reference the pretreatment sum diameter. Percentage of participants = (number of participants who had CR or PR) / (number of participants treated) * 100.

End point type	Secondary
----------------	-----------

End point timeframe:

Randomization to Objective PD or Death Up to 23 Months

End point values	Olaratumab (IMC-3G3) + Mitoxantrone	Mitoxantrone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30 ^[7]	32 ^[8]		
Units: percentage of participants				
number (confidence interval 95%)	10 (3.5 to 25.6)	3.1 (0.6 to 15.7)		

Notes:

[7] - All randomized participants who received at least ≥ 1 dose of study drug and had measurable disease.

[8] - All randomized participants who received at least ≥ 1 dose of study drug and had measurable disease.

Statistical analyses

Statistical analysis title	Statistical Analysis for Best Overall Response
Comparison groups	Mitoxantrone v Olaratumab (IMC-3G3) + Mitoxantrone
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3465
Method	Fisher exact

Secondary: Percentage of participants with a $\geq 50\%$ decrease in Prostate Specific Androgen (PSA) from pretreatment to any time

End point title	Percentage of participants with a $\geq 50\%$ decrease in Prostate Specific Androgen (PSA) from pretreatment to any time
-----------------	--

End point description:

Decrease in PSA $\geq 50\%$ from pretreatment required confirmation no less than 3 weeks after the initial suggestion of response and occurring prior to documentation of PD. Percentage of participants = (number of participants who had $\geq 50\%$ decrease in PSA at any time) / (number of participants treated) * 100.

End point type	Secondary
----------------	-----------

End point timeframe:

Pretreatment to PD Up to 23 Months

End point values	Olaratumab (IMC-3G3) + Mitoxantrone	Mitoxantrone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62 ^[9]	59		
Units: percentage of participants				
number (confidence interval 95%)	22.6 (14 to 34.4)	18.6 (10.7 to 30.4)		

Notes:

[9] - All randomized participants who received ≥ 1 dose of study drug.

Statistical analyses

Statistical analysis title	Statistical Analysis for $\geq 50\%$ Decrease in PSA
Comparison groups	Mitoxantrone v Olaratumab (IMC-3G3) + Mitoxantrone
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6571
Method	Fisher exact

Secondary: Percentage of Participants With a $\geq 30\%$ Decrease in PSA From Pretreatment to Week 12

End point title	Percentage of Participants With a $\geq 30\%$ Decrease in PSA From Pretreatment to Week 12
End point description:	Percentage of participants = (number of participants who had $\geq 30\%$ decrease in PSA at Week 12) / (number of participants treated) * 100.
End point type	Secondary
End point timeframe:	Pretreatment through Week 12

End point values	Olaratumab (IMC-3G3) + Mitoxantrone	Mitoxantrone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62 ^[10]	59 ^[11]		
Units: percentage of participants				
number (confidence interval 95%)	22.6 (14 to 34.4)	16.9 (9.5 to 28.5)		

Notes:

[10] - All randomized participants who received ≥ 1 dose of study drug.

[11] - All randomized participants who received ≥ 1 dose of study drug.

Statistical analyses

Statistical analysis title	Statistical Analysis for $\geq 30\%$ Decrease in PSA
Comparison groups	Mitoxantrone v Olaratumab (IMC-3G3) + Mitoxantrone

Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4986
Method	Fisher exact

Secondary: Summary Listing of Participants Reporting Treatment-Emergent Adverse Events (TEAE)

End point title	Summary Listing of Participants Reporting Treatment-Emergent Adverse Events (TEAE)
-----------------	--

End point description:

Data presented are the number of participants who experienced serious adverse events (SAEs) and other nonserious adverse events (AEs). For participants in mitoxantrone group who had PD and chose optional IMC-3G3 follow-on treatment, the baseline was defined as the last assessment prior to the start of the olaratumab treatment. A summary of SAEs and other nonserious AEs, regardless of causality, is located in the Reported Adverse Events section.

End point type	Secondary
----------------	-----------

End point timeframe:

From Start of Treatment Through Study Completion Up to 36 months

End point values	Olaratumab (IMC-3G3) + Mitoxantrone	Mitoxantrone	Optional Olaratumab Monotherapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	62 ^[12]	59	19 ^[13]	
Units: participants				
number (not applicable)				
SAEs	26	21	6	
AEs	52	51	15	

Notes:

[12] - All randomized participants who received at least 1 dose of study drug.

[13] - All randomized participants who received at least 1 dose of study drug.

Statistical analyses

No statistical analyses for this end point

Secondary: PFS based on baseline Circulating Tumor Cells (CTC) counts

End point title	PFS based on baseline Circulating Tumor Cells (CTC) counts
-----------------	--

End point description:

High expression (HE) of CTC was defined as having CTC counts ≥ 5 cells/7.5 milliliter (mL) and low expression (LE) of CTC was defined as having CTC counts < 5 cells/7.5 mL. PFS is measured from randomization to the earliest date of the following events: PD according to RECIST criteria v. 1.1, is a $\geq 20\%$ increase in the sum diameter of the target lesions taking as reference the smallest sum on study and an absolute increase in the sum diameter of ≥ 5 mm, the appearance of 1 or more new lesions and/or unequivocal progression of existing nontarget lesions, unequivocal evidence of progression by bone scan, clinical progression or death from any cause.

End point type	Secondary
----------------	-----------

End point timeframe:

Randomization to Measured PD or Death Due to Any Cause Up to 23 Months

End point values	PFS Olaratumab + Mitoxantrone + Mitoxantrone (LE)	PFS Olaratumab + Mitoxantrone and Mitoxantrone (HE)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	118 ^[14]	118 ^[15]		
Units: months				
median (confidence interval 95%)	3.61 (2.33 to 7.16)	2.3 (2.14 to 2.37)		

Notes:

[14] - Low expression CTC counts

[15] - High expression CTC counts

Statistical analyses

No statistical analyses for this end point

Secondary: OS Based on Baseline CTC Counts

End point title	OS Based on Baseline CTC Counts
End point description:	
HE of CTC was defined as having CTC counts ≥ 5 cells/7.5 mL and LE of CTC was defined as having CTC counts < 5 cells/7.5 mL. OS was defined as the time from the date of randomization to the date of death from any cause.	
End point type	Secondary
End point timeframe:	
Randomization to Death Due to Any Cause Up to 36 Months	

End point values	OS Olaratumab + Mitoxantrone + Mitoxantrone (LE)	OS Olaratumab + Mitoxantrone and Mitoxantrone (HE)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	118 ^[16]	118 ^[17]		
Units: months				
median (confidence interval 95%)	19.02 (12.32 to 9999)	11.56 (7.1 to 13.4)		

Notes:

[16] - Low expression CTC counts. 95% CI upper limit is not available due to not statistically estimable.

[17] - High expression CTC counts

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with negative platelet-Derived growth factor receptor alpha (PDGFR α) protein expression by immunohistochemistry (IHC)

End point title	Number of participants with negative platelet-Derived growth factor receptor alpha (PDGFRα) protein expression by immunohistochemistry (IHC)
End point description: PDGFRα protein expression (pretreatment) by IHC was assessed in tumor cells, and was provided as a dichotomous variable with "positive" and "negative" expression. "Positive" corresponds to weak intensity membranous staining comprising greater than 30% of the tumor and/or moderate to strong intensity membranous staining comprising greater than 5% of the tumor. "Negative" corresponds to staining that does not meet these requirements.	
End point type	Secondary
End point timeframe: Baseline	

End point values	Olaratumab (IMC-3G3) + Mitoxantrone	Mitoxantrone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14 ^[18]	9 ^[19]		
Units: participants				
number (not applicable)	14	9		

Notes:

[18] - All randomized participants who had tissue specimens from the initial diagnosis for PDGFRα.

[19] - All randomized participants who had tissue specimens from the initial diagnosis for PDGFRα.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Anti-Olaratumab Antibody Assessment (immunogenicity)

End point title	Percentage of Participants with Anti-Olaratumab Antibody Assessment (immunogenicity)
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: From Start of Treatment up to 9 Months	

End point values	Olaratumab (IMC-3G3) + Mitoxantrone	Mitoxantrone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52 ^[20]	11 ^[21]		
Units: percent of participants				
number (not applicable)	3.8	0		

Notes:

[20] - All randomized participants who had evaluable baseline and evaluable post-baseline antibody data.

[21] - All randomized participants who had evaluable baseline and evaluable post-baseline antibody data.

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum concentration (Cmax) of Olaratumab cycles 1, 2 and 3

End point title	Maximum concentration (Cmax) of Olaratumab cycles 1, 2 and 3
-----------------	--

End point description:

End point type	Secondary
----------------	-----------

End point timeframe:

Day 1 of Cycles 1, 2 and 3, and Day 8 of Cycles 1 and 3 (21-day cycle)

End point values	Olaratumab (IMC-3G3) + Mitoxantrone	Mitoxantrone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[22]	0 ^[23]		
Units: number				
number (not applicable)				

Notes:

[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

Other pre-specified: Number of participants who died during study

End point title	Number of participants who died during study
-----------------	--

End point description:

End point type	Other pre-specified
----------------	---------------------

End point timeframe:

From Start of Treatment through Study Completion up to 36 Months

End point values	Olaratumab (IMC-3G3) + Mitoxantrone	Mitoxantrone	Optional Olaratumab Monotherapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	62 ^[24]	59 ^[25]	19 ^[26]	
Units: participants				
number (not applicable)				
Due to PD	43	27	12	
Due to AEs	4	3	1	
Due to Other reasons	3	2	1	

Notes:

[24] - All randomized participants who received ≥ 1 dose of study drug.

[25] - All randomized participants who received ≥ 1 dose of study drug.

[26] - All randomized participants who received ≥ 1 dose of study drug.

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-JGDD

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

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	13.0
--------------------	------

Reporting groups

Reporting group title	Olaratumab + Mitoxantrone
-----------------------	---------------------------

Reporting group description: -

Reporting group title	Mitoxantrone
-----------------------	--------------

Reporting group description: -

Reporting group title	Optional Olaratumab Monotherapy
-----------------------	---------------------------------

Reporting group description:

Participants who experienced PD had the option to receive olaratumab monotherapy treatment. 15 mg/kg olaratumab was administered IV on Days 1 and 8 of each 21-day cycle with 5 mg prednisone PO BID on each day. Participants received treatment until withdrawal criteria were met. These participants are a subset of the control arm.

Serious adverse events	Olaratumab + Mitoxantrone	Mitoxantrone	Optional Olaratumab Monotherapy
Total subjects affected by serious adverse events			
subjects affected / exposed	26 / 62 (41.94%)	21 / 59 (35.59%)	6 / 19 (31.58%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
circulatory collapse			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	0 / 62 (0.00%)	1 / 59 (1.69%)	0 / 19 (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
deep vein thrombosis			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	2 / 62 (3.23%)	1 / 59 (1.69%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			

asthenia				
alternative dictionary used: MedDRA 13.0				
subjects affected / exposed	1 / 62 (1.61%)	0 / 59 (0.00%)	1 / 19 (5.26%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0	
fatigue				
alternative dictionary used: MedDRA 13.0				
subjects affected / exposed	0 / 62 (0.00%)	1 / 59 (1.69%)	0 / 19 (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	
general physical health deterioration				
alternative dictionary used: MedDRA 13.0				
subjects affected / exposed	1 / 62 (1.61%)	1 / 59 (1.69%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0	
localised oedema				
alternative dictionary used: MedDRA 13.0				
subjects affected / exposed	0 / 62 (0.00%)	1 / 59 (1.69%)	0 / 19 (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	
multi-organ failure				
alternative dictionary used: MedDRA 13.0				
subjects affected / exposed	1 / 62 (1.61%)	0 / 59 (0.00%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0	
oedema peripheral				
alternative dictionary used: MedDRA 13.0				
subjects affected / exposed	0 / 62 (0.00%)	1 / 59 (1.69%)	0 / 19 (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	
pain				
alternative dictionary used: MedDRA 13.0				

subjects affected / exposed	0 / 62 (0.00%)	1 / 59 (1.69%)	2 / 19 (10.53%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
anaphylactic reaction			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	2 / 62 (3.23%)	0 / 59 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
anaphylactic shock			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	1 / 62 (1.61%)	0 / 59 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypersensitivity			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	1 / 62 (1.61%)	0 / 59 (0.00%)	0 / 19 (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
Respiratory, thoracic and mediastinal disorders			
pleural effusion			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	1 / 62 (1.61%)	0 / 59 (0.00%)	0 / 19 (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
pulmonary embolism			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	3 / 62 (4.84%)	0 / 59 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pulmonary infarction			
alternative dictionary used: MedDRA 13.0			

subjects affected / exposed	1 / 62 (1.61%)	0 / 59 (0.00%)	0 / 19 (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
Psychiatric disorders			
alcoholism			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	0 / 62 (0.00%)	1 / 59 (1.69%)	0 / 19 (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
Investigations			
general physical condition abnormal			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	0 / 62 (0.00%)	1 / 59 (1.69%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
cystitis radiation			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	1 / 62 (1.61%)	0 / 59 (0.00%)	0 / 19 (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
femur fracture			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	1 / 62 (1.61%)	0 / 59 (0.00%)	0 / 19 (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
incorrect dose administered			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	1 / 62 (1.61%)	0 / 59 (0.00%)	0 / 19 (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
subdural haematoma			
alternative dictionary used: MedDRA 13.0			

subjects affected / exposed	1 / 62 (1.61%)	0 / 59 (0.00%)	0 / 19 (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
Cardiac disorders			
atrial fibrillation			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	2 / 62 (3.23%)	1 / 59 (1.69%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
atrial flutter			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	1 / 62 (1.61%)	0 / 59 (0.00%)	0 / 19 (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
cardiac arrest			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	0 / 62 (0.00%)	0 / 59 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
cardiac failure chronic			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	1 / 62 (1.61%)	0 / 59 (0.00%)	0 / 19 (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
cardiac failure congestive			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	1 / 62 (1.61%)	0 / 59 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
congestive cardiomyopathy			
alternative dictionary used: MedDRA 13.0			

subjects affected / exposed	1 / 62 (1.61%)	0 / 59 (0.00%)	0 / 19 (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
myocardial ischaemia			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	0 / 62 (0.00%)	1 / 59 (1.69%)	0 / 19 (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
Nervous system disorders			
cerebral haemorrhage			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	0 / 62 (0.00%)	1 / 59 (1.69%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
cerebrovascular accident			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	1 / 62 (1.61%)	0 / 59 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
depressed level of consciousness			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	1 / 62 (1.61%)	0 / 59 (0.00%)	0 / 19 (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
facial paresis			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	1 / 62 (1.61%)	0 / 59 (0.00%)	0 / 19 (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
ischaemic stroke			
alternative dictionary used: MedDRA 13.0			

subjects affected / exposed	1 / 62 (1.61%)	0 / 59 (0.00%)	0 / 19 (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
muscle spasticity			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	1 / 62 (1.61%)	0 / 59 (0.00%)	0 / 19 (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
paraparesis			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	1 / 62 (1.61%)	0 / 59 (0.00%)	0 / 19 (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
paraplegia			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	1 / 62 (1.61%)	0 / 59 (0.00%)	0 / 19 (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
spinal cord compression			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	1 / 62 (1.61%)	2 / 59 (3.39%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
agranulocytosis			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	0 / 62 (0.00%)	1 / 59 (1.69%)	0 / 19 (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
anaemia			
alternative dictionary used: MedDRA 13.0			

subjects affected / exposed	5 / 62 (8.06%)	4 / 59 (6.78%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	1 / 5	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
anaemia of malignant disease alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	1 / 62 (1.61%)	0 / 59 (0.00%)	0 / 19 (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
febrile neutropenia alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	1 / 62 (1.61%)	1 / 59 (1.69%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
leukopenia alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	0 / 62 (0.00%)	2 / 59 (3.39%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
neutropenia alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	2 / 62 (3.23%)	3 / 59 (5.08%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	4 / 4	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pancytopenia alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	1 / 62 (1.61%)	0 / 59 (0.00%)	0 / 19 (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
thrombocytopenia alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	3 / 62 (4.84%)	0 / 59 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Ear and labyrinth disorders vertigo alternative dictionary used: MedDRA 13.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 62 (1.61%) 1 / 1 0 / 0	 0 / 59 (0.00%) 0 / 0 0 / 0	 0 / 19 (0.00%) 0 / 0 0 / 0
Gastrointestinal disorders abdominal pain alternative dictionary used: MedDRA 13.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 62 (0.00%) 0 / 0 0 / 0	 1 / 59 (1.69%) 0 / 1 0 / 0	 1 / 19 (5.26%) 0 / 1 0 / 0
nausea alternative dictionary used: MedDRA 13.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 62 (0.00%) 0 / 0 0 / 0	 1 / 59 (1.69%) 0 / 1 0 / 0	 1 / 19 (5.26%) 0 / 1 0 / 0
periodontitis alternative dictionary used: MedDRA 13.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 62 (0.00%) 0 / 0 0 / 0	 1 / 59 (1.69%) 0 / 1 0 / 0	 0 / 19 (0.00%) 0 / 0 0 / 0
Renal and urinary disorders hydronephrosis alternative dictionary used: MedDRA 13.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 62 (0.00%) 0 / 0 0 / 0	 1 / 59 (1.69%) 0 / 1 0 / 0	 0 / 19 (0.00%) 0 / 0 0 / 0
renal failure acute alternative dictionary used: MedDRA 13.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 62 (1.61%) 0 / 1 0 / 0	 0 / 59 (0.00%) 0 / 0 0 / 0	 0 / 19 (0.00%) 0 / 0 0 / 0
urinary tract obstruction			

alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	0 / 62 (0.00%)	1 / 59 (1.69%)	0 / 19 (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
Musculoskeletal and connective tissue disorders			
bone pain			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	1 / 62 (1.61%)	0 / 59 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
muscular weakness			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	1 / 62 (1.61%)	0 / 59 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pain in extremity			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	1 / 62 (1.61%)	0 / 59 (0.00%)	0 / 19 (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
Infections and infestations			
bronchopneumonia			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	0 / 62 (0.00%)	1 / 59 (1.69%)	0 / 19 (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
erysipelas			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	1 / 62 (1.61%)	0 / 59 (0.00%)	0 / 19 (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
gastroenteritis escherichia coli			
alternative dictionary used: MedDRA 13.0			

subjects affected / exposed	1 / 62 (1.61%)	0 / 59 (0.00%)	0 / 19 (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
pneumonia			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	1 / 62 (1.61%)	3 / 59 (5.08%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
rectal abscess			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	0 / 62 (0.00%)	0 / 59 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
respiratory tract infection			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	2 / 62 (3.23%)	1 / 59 (1.69%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
septic shock			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	1 / 62 (1.61%)	0 / 59 (0.00%)	0 / 19 (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 13.0			
subjects affected / exposed	1 / 62 (1.61%)	0 / 59 (0.00%)	0 / 19 (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
urosepsis			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	0 / 62 (0.00%)	1 / 59 (1.69%)	0 / 19 (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

Metabolism and nutrition disorders			
cachexia			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	1 / 62 (1.61%)	0 / 59 (0.00%)	0 / 19 (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
dehydration			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	0 / 62 (0.00%)	1 / 59 (1.69%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 1	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 + Mitoxantrone	Mitoxantrone	Optional Olaratumab Monotherapy
Total subjects affected by non-serious adverse events			
subjects affected / exposed	52 / 62 (83.87%)	51 / 59 (86.44%)	15 / 19 (78.95%)
Vascular disorders			
hypertension			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	5 / 62 (8.06%)	2 / 59 (3.39%)	0 / 19 (0.00%)
occurrences (all)	7	6	0
hypotension			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	0 / 62 (0.00%)	3 / 59 (5.08%)	0 / 19 (0.00%)
occurrences (all)	0	3	0
thrombosis			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	0 / 62 (0.00%)	0 / 59 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 13.0			

subjects affected / exposed	18 / 62 (29.03%)	13 / 59 (22.03%)	5 / 19 (26.32%)
occurrences (all)	39	23	5
fatigue			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	11 / 62 (17.74%)	11 / 59 (18.64%)	3 / 19 (15.79%)
occurrences (all)	11	13	3
infusion related reaction			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	1 / 62 (1.61%)	0 / 59 (0.00%)	2 / 19 (10.53%)
occurrences (all)	1	0	3
oedema peripheral			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	6 / 62 (9.68%)	4 / 59 (6.78%)	1 / 19 (5.26%)
occurrences (all)	8	4	1
pyrexia			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	4 / 62 (6.45%)	7 / 59 (11.86%)	1 / 19 (5.26%)
occurrences (all)	8	7	1
Reproductive system and breast disorders			
pelvic pain			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	3 / 62 (4.84%)	2 / 59 (3.39%)	2 / 19 (10.53%)
occurrences (all)	3	2	2
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	4 / 62 (6.45%)	6 / 59 (10.17%)	0 / 19 (0.00%)
occurrences (all)	4	6	0
dyspnoea			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	4 / 62 (6.45%)	4 / 59 (6.78%)	1 / 19 (5.26%)
occurrences (all)	4	5	1
pleural effusion			
alternative dictionary used: MedDRA 13.0			

subjects affected / exposed occurrences (all)	2 / 62 (3.23%) 2	1 / 59 (1.69%) 2	1 / 19 (5.26%) 1
Psychiatric disorders anxiety alternative dictionary used: MedDRA 13.0 subjects affected / exposed occurrences (all)	0 / 62 (0.00%) 0	2 / 59 (3.39%) 2	1 / 19 (5.26%) 1
depression alternative dictionary used: MedDRA 13.0 subjects affected / exposed occurrences (all)	2 / 62 (3.23%) 2	1 / 59 (1.69%) 1	1 / 19 (5.26%) 1
Investigations aspartate aminotransferase increased alternative dictionary used: MedDRA 13.0 subjects affected / exposed occurrences (all)	1 / 62 (1.61%) 1	1 / 59 (1.69%) 1	1 / 19 (5.26%) 1
ejection fraction decreased alternative dictionary used: MedDRA 13.0 subjects affected / exposed occurrences (all)	1 / 62 (1.61%) 1	3 / 59 (5.08%) 3	0 / 19 (0.00%) 0
gamma-glutamyltransferase increased alternative dictionary used: MedDRA 13.0 subjects affected / exposed occurrences (all)	2 / 62 (3.23%) 2	3 / 59 (5.08%) 5	0 / 19 (0.00%) 0
weight decreased alternative dictionary used: MedDRA 13.0 subjects affected / exposed occurrences (all)	2 / 62 (3.23%) 2	5 / 59 (8.47%) 6	0 / 19 (0.00%) 0
Nervous system disorders dizziness alternative dictionary used: MedDRA 13.0 subjects affected / exposed occurrences (all)	2 / 62 (3.23%) 3	3 / 59 (5.08%) 4	0 / 19 (0.00%) 0
dysgeusia alternative dictionary used:			

MedDRA 13.0			
subjects affected / exposed	2 / 62 (3.23%)	3 / 59 (5.08%)	0 / 19 (0.00%)
occurrences (all)	2	4	0
headache			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	4 / 62 (6.45%)	5 / 59 (8.47%)	1 / 19 (5.26%)
occurrences (all)	6	17	1
paraesthesia			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	1 / 62 (1.61%)	3 / 59 (5.08%)	0 / 19 (0.00%)
occurrences (all)	1	3	0
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	17 / 62 (27.42%)	15 / 59 (25.42%)	3 / 19 (15.79%)
occurrences (all)	41	33	4
leukopenia			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	9 / 62 (14.52%)	8 / 59 (13.56%)	0 / 19 (0.00%)
occurrences (all)	25	13	0
neutropenia			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	19 / 62 (30.65%)	11 / 59 (18.64%)	0 / 19 (0.00%)
occurrences (all)	44	28	0
thrombocytopenia			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	8 / 62 (12.90%)	6 / 59 (10.17%)	1 / 19 (5.26%)
occurrences (all)	19	17	1
Ear and labyrinth disorders			
vertigo			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	2 / 62 (3.23%)	4 / 59 (6.78%)	0 / 19 (0.00%)
occurrences (all)	2	6	0
Gastrointestinal disorders			

abdominal pain			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	2 / 62 (3.23%)	2 / 59 (3.39%)	1 / 19 (5.26%)
occurrences (all)	2	3	1
abdominal pain upper			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	0 / 62 (0.00%)	3 / 59 (5.08%)	0 / 19 (0.00%)
occurrences (all)	0	4	0
cheilitis			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	0 / 62 (0.00%)	0 / 59 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
constipation			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	5 / 62 (8.06%)	11 / 59 (18.64%)	3 / 19 (15.79%)
occurrences (all)	6	14	4
diarrhoea			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	12 / 62 (19.35%)	7 / 59 (11.86%)	0 / 19 (0.00%)
occurrences (all)	15	8	0
dyspepsia			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	0 / 62 (0.00%)	5 / 59 (8.47%)	0 / 19 (0.00%)
occurrences (all)	0	6	0
dysphagia			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	0 / 62 (0.00%)	1 / 59 (1.69%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
haemorrhoidal haemorrhage			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	0 / 62 (0.00%)	0 / 59 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
nausea			
alternative dictionary used: MedDRA 13.0			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>15 / 62 (24.19%)</p> <p>19</p>	<p>14 / 59 (23.73%)</p> <p>19</p>	<p>2 / 19 (10.53%)</p> <p>2</p>
<p>vomiting</p> <p>alternative dictionary used: MedDRA 13.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>5 / 62 (8.06%)</p> <p>5</p>	<p>3 / 59 (5.08%)</p> <p>3</p>	<p>1 / 19 (5.26%)</p> <p>1</p>
<p>Skin and subcutaneous tissue disorders</p> <p>hypoesthesia facial</p> <p>alternative dictionary used: MedDRA 13.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>0 / 62 (0.00%)</p> <p>0</p>	<p>0 / 59 (0.00%)</p> <p>0</p>	<p>1 / 19 (5.26%)</p> <p>1</p>
<p>rash</p> <p>alternative dictionary used: MedDRA 13.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>0 / 62 (0.00%)</p> <p>0</p>	<p>2 / 59 (3.39%)</p> <p>2</p>	<p>2 / 19 (10.53%)</p> <p>2</p>
<p>skin disorder</p> <p>alternative dictionary used: MedDRA 13.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>0 / 62 (0.00%)</p> <p>0</p>	<p>0 / 59 (0.00%)</p> <p>0</p>	<p>1 / 19 (5.26%)</p> <p>1</p>
<p>Renal and urinary disorders</p> <p>haematuria</p> <p>alternative dictionary used: MedDRA 13.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>2 / 62 (3.23%)</p> <p>3</p>	<p>4 / 59 (6.78%)</p> <p>5</p>	<p>0 / 19 (0.00%)</p> <p>0</p>
<p>pollakiuria</p> <p>alternative dictionary used: MedDRA 13.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>0 / 62 (0.00%)</p> <p>0</p>	<p>0 / 59 (0.00%)</p> <p>0</p>	<p>1 / 19 (5.26%)</p> <p>2</p>
<p>urinary incontinence</p> <p>alternative dictionary used: MedDRA 13.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>1 / 62 (1.61%)</p> <p>1</p>	<p>4 / 59 (6.78%)</p> <p>4</p>	<p>0 / 19 (0.00%)</p> <p>0</p>
<p>urinary retention</p> <p>alternative dictionary used: MedDRA 13.0</p>		

subjects affected / exposed	0 / 62 (0.00%)	0 / 59 (0.00%)	3 / 19 (15.79%)
occurrences (all)	0	0	4
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	7 / 62 (11.29%)	3 / 59 (5.08%)	0 / 19 (0.00%)
occurrences (all)	7	6	0
back pain			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	6 / 62 (9.68%)	7 / 59 (11.86%)	2 / 19 (10.53%)
occurrences (all)	8	8	2
bone pain			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	7 / 62 (11.29%)	5 / 59 (8.47%)	1 / 19 (5.26%)
occurrences (all)	10	5	1
flank pain			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	0 / 62 (0.00%)	1 / 59 (1.69%)	1 / 19 (5.26%)
occurrences (all)	0	2	1
muscle atrophy			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	0 / 62 (0.00%)	0 / 59 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
muscle spasms			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	4 / 62 (6.45%)	1 / 59 (1.69%)	0 / 19 (0.00%)
occurrences (all)	5	1	0
musculoskeletal pain			
alternative dictionary used: MedDRA 13.0			
subjects affected / exposed	1 / 62 (1.61%)	4 / 59 (6.78%)	2 / 19 (10.53%)
occurrences (all)	1	4	2
pain in extremity			
alternative dictionary used: MedDRA 13.0			

subjects affected / exposed occurrences (all)	7 / 62 (11.29%) 7	3 / 59 (5.08%) 4	0 / 19 (0.00%) 0
Infections and infestations urinary tract infection alternative dictionary used: MedDRA 13.0 subjects affected / exposed occurrences (all)	2 / 62 (3.23%) 2	1 / 59 (1.69%) 2	1 / 19 (5.26%) 1
Metabolism and nutrition disorders decreased appetite alternative dictionary used: MedDRA 13.0 subjects affected / exposed occurrences (all) hypokalaemia alternative dictionary used: MedDRA 13.0 subjects affected / exposed occurrences (all) hypovitaminosis alternative dictionary used: MedDRA 13.0 subjects affected / exposed occurrences (all) vitamin b12 deficiency alternative dictionary used: MedDRA 13.0 subjects affected / exposed occurrences (all)	11 / 62 (17.74%) 15 1 / 62 (1.61%) 1 0 / 62 (0.00%) 0 0 / 62 (0.00%) 0	6 / 59 (10.17%) 10 1 / 59 (1.69%) 1 0 / 59 (0.00%) 0 1 / 59 (1.69%) 1	3 / 19 (15.79%) 5 1 / 19 (5.26%) 1 1 / 19 (5.26%) 1 1 / 19 (5.26%) 1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 September 2010	<p>Protocol Version 2.0 dated 28-Sep-2010. Changes from Version 1.0</p> <ul style="list-style-type: none">• Updated to reflect new data— the 39-week toxicology study in monkeys— that was presented in the updated Investigator's Brochure (V5.1)• Added updated patient disposition and safety information for all clinical IMC-3G3 studies presented in the updated Investigator's Brochure (V5.1)• Body surface area to be measured only on Day 1 for patients with scheduled mitoxantrone administration• Per request by the German Health Authority, a description of the independent data monitoring committee (IDMC) provided in-text• Various administrative changes for further clarity

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Efficacy analysis for the follow-on treatment is exploratory, therefore, efficacy analysis for follow-on treatment are not included in this clinical trial results.

Notes: