



Clinical trial results:

GOAL trial: Rescue treatment with the monoclonal anti CD20-antibody Obinutuzumab (GA101) in combination with PixantrOne for the treatment of patients with relapsed Aggressive B-cell Lymphoma

Summary

EudraCT number	2014-004780-21
Trial protocol	DE
Global end of trial date	02 January 2022

Results information

Result version number	v1 (current)
This version publication date	22 June 2023
First version publication date	22 June 2023

Trial information

Trial identification

Sponsor protocol code	ETN-1-GOAL
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University Medical Center of the Johannes Gutenberg
Sponsor organisation address	Langenbeckstr 2, Mainz, Germany, 55131
Public contact	Georg Hess, University Medical Center of the Johannes Gutenberg, 0049 6131175040, ruckes@izks-mainz.de
Scientific contact	Georg Hess, University Medical Center of the Johannes Gutenberg, 6131179919 6131175040, ruckes@izks-mainz.de

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	02 May 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 May 2021
Global end of trial reached?	Yes
Global end of trial date	02 January 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To evaluate the overall response rate (ORR) of the combination after completion or termination of trial treatment

Protection of trial subjects:

Ethics approval, authority approval

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 July 2015
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	Germany: 70
Worldwide total number of subjects	70
EEA total number of subjects	70

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)	19
From 65 to 84 years	50
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

70 patients were enrolled

68 patients were analyzed for efficacy and safety

60 patients were analyzed mITT (available tumor assessment)

42 patients were analyzed within GCB evaluation

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	70
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Number of subjects completed	68
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Pre-assignment subject non-completion reasons

Reason: Number of subjects	Did not receive stdy medication: 2
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Period 1

Period 1 title	Treatment Period (overall period)
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Is this the baseline period?	Yes
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Allocation method	Not applicable
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Blinding used	Not blinded
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Blinding implementation details:

Not applicable, single-arm trial

Arms

Arm title	Obinutuzumab+Pixantrone
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Arm description:

Patients received 1000 mg of Obinutuzumab on days 1, 8 and 15 (first cycle) or day 1 of any following cycle in combination with 50 mg/m² Pixantrone on days 1, 8 and 15 of a 28-day cycle for up to six cycles.

Arm type	Experimental
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Investigational medicinal product name	Obinutuzumab
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Investigational medicinal product code	
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Other name	Gazyvaro
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Pharmaceutical forms	Tablet
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Routes of administration	Oral use
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Dosage and administration details:

1000 mg of Obinutuzumab on days 1, 8 and 15 (first cycle) or day 1 of any following cycle

Investigational medicinal product name	Pixantrone
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Investigational medicinal product code	
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Other name	Pixuvri
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Pharmaceutical forms	Infusion
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Routes of administration	Infusion
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Dosage and administration details:

50 mg/m² Pixantrone on days 1, 8 and 15 of a 28-day cycle

Number of subjects in period 1^[1]	Obinutuzumab+Pixa ntrone
Started	68
Completed	20
Not completed	48
Adverse event, serious fatal	3
Consent withdrawn by subject	2
Adverse event, non-fatal	10
Unspecified	2
Disease Progression	31

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Only the number of patients receiving study medication were analyzed.

Baseline characteristics

Reporting groups

Reporting group title	Treatment Period
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Reporting group description: -

Reporting group values	Treatment Period	Total	
Number of subjects	68	68	
Age categorical			
Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Units: years			
arithmetic mean	70.49		
standard deviation	± 11.67	-	
Gender categorical			
Units: Subjects			
Female	37	37	
Male	31	31	
Current Lymphoma Stage			
Units: Subjects			
Stage I	8	8	
Stage II	13	13	
Stage III	14	14	
Stage IV	32	32	
Missing	1	1	
Histologically proven type of lymphoma			
Units: Subjects			
Diffuse large B-cell lymphoma	49	49	
Follicular lymphoma grade IIIB	1	1	
Follicular lymphoma grade IIIA	3	3	
Follicular lymphoma grade II	3	3	
Follicular lymphoma grade I	4	4	
Other	8	8	
Histologically proven type of lymphoma			
Histologically proven type of lymphoma at screening			
Units: Subjects			
Diffuse large B-cell lymphoma	52	52	
Follicular lymphoma grade IIIB	2	2	

Transformed to DLBCL	8	8	
Transformed to FL3B	1	1	
Transformed to burkitt-like lymphoma	1	1	
Other	4	4	
Prior lymphoma treatment - chemotherapies			
Units: Subjects			
=1	19	19	
=2	27	27	
=3	13	13	
>3	9	9	
Prior lymphoma treatment - antibodies			
Units: Subjects			
=1	16	16	
=2	17	17	
>2	35	35	
Prior lymphoma treatment - novel agents			
Units: Subjects			
None	64	64	
=1	4	4	
Prior lymphoma treatment - consolidation			
Units: Subjects			
None	56	56	
=1	11	11	
=2	1	1	
Best response to most recent prior therapy			
Units: Subjects			
CR	14	14	
CRu	1	1	
PR	14	14	
SD	3	3	
PD	31	31	
Discontinued	2	2	
Unknown	3	3	

End points

End points reporting groups

Reporting group title	Obinutuzumab+Pixantrone
Reporting group description: Patients received 1000 mg of Obinutuzumab on days 1, 8 and 15 (first cycle) or day 1 of any following cycle in combination with 50 mg/m ² Pixantrone on days 1, 8 and 15 of a 28-day cycle for up to six cycles.	
Subject analysis set title	GEP-profiling
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subjects who took part in the gene expression profiling (GEP). Recent gene expression profiling studies supported the view that DLBCL is heterogeneous, as two major molecular DLBCL subtypes, termed germinal center B-cell-like (GCB) DLBCL and activated B-cell-like (ABC) DLBCL, could be distinguished.	

Primary: Objective Response Rate

End point title	Objective Response Rate ^[1]
End point description:	
End point type	Primary
End point timeframe: 44 weeks	
Notes: [1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: This is only a single arm trial.	

End point values	Obinutuzumab +Pixantrone	GEP-profiling		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	68	42		
Units: Patients				
Response	24	13		
Non-response	36	29		
Not recorded	8	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival

End point title	Progression-free survival
End point description: Time from first medication intake to first documentation of objective tumor progression or to death due to any cause, whichever occurs first.	
End point type	Secondary
End point timeframe: 44 months	

End point values	Obinutuzumab +Pixantrone			
Subject group type	Reporting group			
Number of subjects analysed	68			
Units: months				
median (confidence interval 95%)	2.8 (2.0 to 6.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival
End point description:	
End point type	Secondary
End point timeframe:	
44 months	

End point values	Obinutuzumab +Pixantrone			
Subject group type	Reporting group			
Number of subjects analysed	68			
Units: months				
median (confidence interval 95%)	8.0 (4.8 to 12.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival GCB

End point title	Progression-free survival GCB
End point description:	
Progression-free survival for the GCB cohort	
End point type	Secondary
End point timeframe:	
44 months	

End point values	GEP-profiling			
Subject group type	Subject analysis set			
Number of subjects analysed	22			
Units: month				
median (confidence interval 95%)	1.8 (1.0 to 6.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival non-GCB

End point title	Progression-free survival non-GCB
End point description:	
End point type	Secondary
End point timeframe:	
44 months	

End point values	GEP-profiling			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: month				
median (confidence interval 95%)	6.5 (2.3 to 999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival GCB

End point title	Overall Survival GCB
End point description:	
End point type	Secondary
End point timeframe:	
44 months	

End point values	GEP-profiling			
Subject group type	Subject analysis set			
Number of subjects analysed	22			
Units: month				
median (confidence interval 95%)	5.2 (1.8 to 10.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival non-GCB

End point title	Overall Survival non-GCB
End point description:	
End point type	Secondary
End point timeframe:	
44 months	

End point values	GEP-profiling			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: month				
median (confidence interval 95%)	99 (7.2 to 999)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

24 weeks (6 treatment cycles)

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.0
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Reporting groups

Reporting group title	Obinutuzumab+Pixantrone
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Reporting group description: -

Serious adverse events	Obinutuzumab+Pixantrone		
Total subjects affected by serious adverse events			
subjects affected / exposed	58 / 68 (85.29%)		
number of deaths (all causes)	45		
number of deaths resulting from adverse events	16		
Investigations			
Amylase decreased			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Lipase increased			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neutrophil count decreased			
subjects affected / exposed	2 / 68 (2.94%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Platelet count decreased			

subjects affected / exposed	1 / 68 (1.47%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
White blood cell count decreased			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	2 / 68 (2.94%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	1 / 1		
Lung neoplasm malignant			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Non-Hodgkin's lymphoma			
subjects affected / exposed	7 / 68 (10.29%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 7		
Injury, poisoning and procedural complications			
Ulna fracture			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Bicytopenia			

subjects affected / exposed	1 / 68 (1.47%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	3 / 68 (4.41%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		
Granulocytopenia			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Leukopenia			
subjects affected / exposed	22 / 68 (32.35%)		
occurrences causally related to treatment / all	1 / 29		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	31 / 68 (45.59%)		
occurrences causally related to treatment / all	1 / 37		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	8 / 68 (11.76%)		
occurrences causally related to treatment / all	1 / 12		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	4 / 68 (5.88%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 4		
Fatigue			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General physical health deterioration			

subjects affected / exposed	1 / 68 (1.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Malaise			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pain			
subjects affected / exposed	4 / 68 (5.88%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	3 / 68 (4.41%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Subileus			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholestasis			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			

Erysipelas				
subjects affected / exposed	1 / 68 (1.47%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Escherichia sepsis				
subjects affected / exposed	1 / 68 (1.47%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	3 / 68 (4.41%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 1			
Influenza				
subjects affected / exposed	1 / 68 (1.47%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Peritonitis				
subjects affected / exposed	1 / 68 (1.47%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pharyngitis				
subjects affected / exposed	1 / 68 (1.47%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	6 / 68 (8.82%)			
occurrences causally related to treatment / all	1 / 6			
deaths causally related to treatment / all	0 / 1			
Sepsis				
subjects affected / exposed	2 / 68 (2.94%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 1			
Urinary tract infection				

subjects affected / exposed	1 / 68 (1.47%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 68 (1.47%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Obinutuzumab+Pixa ntrone		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	68 / 68 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Non-Hodgkin's lymphoma			
subjects affected / exposed	7 / 68 (10.29%)		
occurrences (all)	7		
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 68 (7.35%)		
occurrences (all)	5		
Hypotension			
subjects affected / exposed	4 / 68 (5.88%)		
occurrences (all)	4		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	19 / 68 (27.94%)		
occurrences (all)	22		
General physical health deterioration			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Oedema peripheral</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pyrexia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>5 / 68 (7.35%)</p> <p>5</p> <p>9 / 68 (13.24%)</p> <p>14</p> <p>6 / 68 (8.82%)</p> <p>7</p> <p>8 / 68 (11.76%)</p> <p>8</p>		
<p>Respiratory, thoracic and mediastinal disorders</p> <p>Cough</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dysphonia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dyspnoea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Oropharyngeal pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pleural effusion</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>10 / 68 (14.71%)</p> <p>11</p> <p>5 / 68 (7.35%)</p> <p>5</p> <p>12 / 68 (17.65%)</p> <p>14</p> <p>4 / 68 (5.88%)</p> <p>4</p> <p>4 / 68 (5.88%)</p> <p>4</p>		
<p>Psychiatric disorders</p> <p>Insomnia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>4 / 68 (5.88%)</p> <p>4</p>		
<p>Investigations</p> <p>Blood creatine increased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Gamma-glutamyltransferase increased</p>	<p>4 / 68 (5.88%)</p> <p>5</p>		

subjects affected / exposed	5 / 68 (7.35%)		
occurrences (all)	11		
Neutrophil count decreased			
subjects affected / exposed	14 / 68 (20.59%)		
occurrences (all)	45		
Platelet count decreased			
subjects affected / exposed	6 / 68 (8.82%)		
occurrences (all)	11		
Troponin I increased			
subjects affected / exposed	4 / 68 (5.88%)		
occurrences (all)	4		
Weight decreased			
subjects affected / exposed	4 / 68 (5.88%)		
occurrences (all)	4		
White blood cell count decreased			
subjects affected / exposed	13 / 68 (19.12%)		
occurrences (all)	48		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	4 / 68 (5.88%)		
occurrences (all)	5		
Nervous system disorders			
Polyneuropathy			
subjects affected / exposed	5 / 68 (7.35%)		
occurrences (all)	6		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	17 / 68 (25.00%)		
occurrences (all)	29		
Leukopenia			
subjects affected / exposed	46 / 68 (67.65%)		
occurrences (all)	86		
Neutropenia			
subjects affected / exposed	46 / 68 (67.65%)		
occurrences (all)	93		
Thrombocytopenia			

subjects affected / exposed occurrences (all)	15 / 68 (22.06%) 34		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 68 (5.88%)		
occurrences (all)	5		
Constipation			
subjects affected / exposed	12 / 68 (17.65%)		
occurrences (all)	13		
Diarrhoea			
subjects affected / exposed	15 / 68 (22.06%)		
occurrences (all)	15		
Nausea			
subjects affected / exposed	14 / 68 (20.59%)		
occurrences (all)	24		
Stomatitis			
subjects affected / exposed	4 / 68 (5.88%)		
occurrences (all)	6		
Vomiting			
subjects affected / exposed	4 / 68 (5.88%)		
occurrences (all)	6		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	12 / 68 (17.65%)		
occurrences (all)	12		
Pruritus			
subjects affected / exposed	5 / 68 (7.35%)		
occurrences (all)	5		
Rash			
subjects affected / exposed	7 / 68 (10.29%)		
occurrences (all)	9		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 68 (7.35%)		
occurrences (all)	5		
Muscle spasms			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pain in extremity</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>5 / 68 (7.35%)</p> <p>6</p> <p>4 / 68 (5.88%)</p> <p>4</p>		
<p>Infections and infestations</p> <p>Infection</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Nasopharyngitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Oral herpes</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pneumonia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Sinusitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Urinary tract infection</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>6 / 68 (8.82%)</p> <p>6</p> <p>5 / 68 (7.35%)</p> <p>5</p> <p>4 / 68 (5.88%)</p> <p>4</p> <p>6 / 68 (8.82%)</p> <p>6</p> <p>4 / 68 (5.88%)</p> <p>4</p> <p>7 / 68 (10.29%)</p> <p>11</p>		
<p>Metabolism and nutrition disorders</p> <p>Decreased appetite</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Hypokalaemia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>4 / 68 (5.88%)</p> <p>4</p> <p>5 / 68 (7.35%)</p> <p>7</p>		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 June 2016	<ul style="list-style-type: none">- Inclusion criteria: Removal of CD20 positive disease.- Inclusion criteria: Change from "LVEF ≥ 45% and normal serum troponin" to "- Adequate cardiac reserve: Serum Troponin level must be consistent with no significant acute or chronic myocardial damage and there should be no evidence of symptomatic".- Clarification of reconstitution process of Pixantrone.- Addition of frequently observed adverse drug reactions of Obinutuzumab and Pixantrone.- Reference to IB-Addendum Number 1, March 2016 of Obinutuzumab concerning precautions for patients considered at risk for Tumor Lysis Syndrome was added.- Observation period for concomitant treatments and adverse events prolonged to 42 days after last administration of trial medication or until the start of a new antineoplastic therapy.- Minor typographic and editorial corrections or clarifications.
06 November 2017	<ul style="list-style-type: none">- Change of manufacturer of Pixantrone.- Addition of frequently observed adverse drug reactions of Obinutuzumab and Pixantrone.- Addition of documentation and reporting of special situations.- Minor typographic and editorial corrections or clarifications.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported