



Clinical trial results:

FIRST LINE THERAPY OF ADVANCED STAGE FOLLICULAR LYMPHOMA IN PATIENTS < 60 YEARS NOT ELIGIBLE FOR STANDARD IMMUNOCHEMOTHERAPY AND ALL PATIENTS 60 YEARS

Prospective randomized evaluation of single agent GA101 versus GA101 plus Bendamustine followed by GA101

Summary

EudraCT number	2016-000755-27
Trial protocol	DE
Global end of trial date	31 December 2022

Results information

Result version number	v1 (current)
This version publication date	29 March 2026
First version publication date	29 March 2026

Trial information

Trial identification

Sponsor protocol code	GABe2016
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03492775
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Klinikum der Universität München
Sponsor organisation address	Marchioninistr 15, München, Germany, 81377
Public contact	Studienzentrale für Hämatologie, LMU Klinikum, Medizinische Klinik III, Studienzentrale für Hämatologie, 0049 89440074900, studyce@med.uni-muenchen.de
Scientific contact	Dr. Christian Schmidt, LMU Klinikum, Medizinische Klinik III, Studienzentrale für Hämatologie, 0049 089440077907, studyce@med.uni-muenchen.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	07 January 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 December 2022
Global end of trial reached?	Yes
Global end of trial date	31 December 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to test the efficacy and toxicity of a combined OBINUTUZUMAB/bendamustine therapy or single agent OBINUTUZUMAB in younger (< 60 years) medically non-fit, 'compromised' patients and in all older patients (≥ 60 years) i. For the assessment of the anti-lymphoma activity the "overall response rate (ORR)" is applied as primary endpoint. Overall response is defined as complete or partial response after 19 – 21 weeks

Protection of trial subjects:

To ensure patients' safety, a Data Safety Monitoring Committee of independent members with pertinent expertise has been established. This international group should review on regular basis safety relevant data and provide an assessment on the patient's overall safety.

The sponsor/sponsor delegated person is under obligation to monitor the progress of the clinical trial with regard to safety-relevant developments and, if necessary, initiate the premature termination of a treatment arm or the entire clinical trial.

A treatment arm or the entire clinical trial must be terminated prematurely if:

- New toxicological or pharmacological SAEs invalidate the earlier benefit-to-risk ratio for the subject.
- Adverse events occurring in such severity and frequency that the proposed schedule can no longer be adhered to.
- The sponsor/coordinating investigator (German LKP) considers that the termination of the trial is necessary.
- Indications arise that the subjects' safety is no longer guaranteed.
- The event-free survival (EFS) is unexpectedly inferior in one of the treatment arms
- An insufficient recruitment rate makes a successful conclusion of the clinical trial appear impossible.
- The reasons for such a decision should be documented in written form
- This decision requires the consultation of the DSMC.

Background therapy:

No Background treatment

Evidence for comparator: -

Actual start date of recruitment	18 September 2017
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	Germany: 46
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Worldwide total number of subjects	46
EEA total number of subjects	46

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)	4
From 65 to 84 years	40
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Start of recruitment 13-DEC-2017, end of recruitment 27-NOV-2020

Pre-assignment

Screening details:

Screening was done according to inclusion/exclusion criteria of the trial protocol. There were 3 screening failures reported during the recruitment period.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

Obinutuzumab single agent.

Patients received obinutuzumab as a flat dose of 1000 mg on day 1 of each of four 28-day cycles and on days 8 and 15 of cycle 1. Patients with at least a stable disease received obinutuzumab as a flat dose of 1000 mg at weeks 21, 29, 37 and 45.

Arm type	Experimental
Investigational medicinal product name	Obinutuzumab
Investigational medicinal product code	
Other name	GAZYVARO
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Obinutuzumab was administered intravenously at a flat dose of 1000 mg on day 1 of each of four 28-day cycles and on days 8 and 15 of cycle 1. Patients with at least a stable disease additionally received obinutuzumab at a flat dose of 1000 mg on day 1 of weeks 21, 29, 37 and 45.

Arm title	Arm B
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Arm description:

Obinutuzumab plus Bendamustine.

Patients received obinutuzumab as a flat dose of 1000 mg on day 1 of each of four 28-day cycles and on days 8 and 15 of cycle 1. Additionally, they received bendamustine at a dose of 70 mg/m² by intravenous infusion on days 1 and 2 of each of four 28-day cycles. Patients with at least a stable disease received obinutuzumab as a flat dose of 1000 mg at weeks 21, 29, 37 and 45.

Arm type	Experimental
Investigational medicinal product name	Obinutuzumab
Investigational medicinal product code	
Other name	GAZYVARO
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Obinutuzumab was administered intravenously at a flat dose of 1000 mg on day 1 of each of four 28-day cycles and on days 8 and 15 of cycle 1. Patients with at least a stable disease additionally received obinutuzumab at a flat dose of 1000 mg on day 1 of weeks 21, 29, 37 and 45.

Investigational medicinal product name	Bendamustine
Investigational medicinal product code	
Other name	Levact, Ribomustine
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Bendamustine was administered at a dose of 70 mg/m² by intravenous infusion on days 1 and 2 of each of four 28-day cycles.

Number of subjects in period 1	Arm A	Arm B
Started	23	23
Completed	23	23

Baseline characteristics

Reporting groups

Reporting group title	Arm A
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Reporting group description:

Obinutuzumab single agent.

Patients received obinutuzumab as a flat dose of 1000 mg on day 1 of each of four 28-day cycles and on days 8 and 15 of cycle 1. Patients with at least a stable disease received obinutuzumab as a flat dose of 1000 mg at weeks 21, 29, 37 and 45.

Reporting group title	Arm B
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Reporting group description:

Obinutuzumab plus Bendamustine.

Patients received obinutuzumab as a flat dose of 1000 mg on day 1 of each of four 28-day cycles and on days 8 and 15 of cycle 1. Additionally, they received bendamustine at a dose of 70 mg/m² by intravenous infusion on days 1 and 2 of each of four 28-day cycles. Patients with at least a stable disease received obinutuzumab as a flat dose of 1000 mg at weeks 21, 29, 37 and 45.

Reporting group values	Arm A	Arm B	Total
Number of subjects	23	23	46
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)	1	3	4
From 65-84 years	20	20	40
85 years and over	2	0	2
Age continuous			
Units: years			
median	76	74	
full range (min-max)	47 to 89	62 to 81	-
Gender categorical			
Units: Subjects			
Female	11	13	24
Male	12	10	22
Histology			
Units: Subjects			
FL grade 1	8	4	12
FL grade 2	12	13	25
FL grade 3a	3	6	9
Ann Arbor stage			
Units: Subjects			
I-II	5	2	7
III-IV	18	21	39
LDH			

Lactate dehydrogenase			
Units: Subjects			
<=upper normal	16	19	35
>upper normal	7	4	11
Hb			
Hemoglobin			
Units: Subjects			
<12g/dL	7	8	15
>=12g/dL	16	15	31
Involved nodal areas			
Units: Subjects			
<=4	15	12	27
>4	8	11	19
FLIPI			
Number of FLIPI risk factors			
Units: Subjects			
FLIPI=0	1	0	1
FLIPI=1	1	2	3
FLIPI=2	9	7	16
FLIPI=3	5	7	12
FLIPI=4	7	5	12
FLIPI=5	0	2	2
ECOG			
Eastern Cooperative Oncology Group Performance Status			
Units: Subjects			
ECOG=0	10	12	22
ECOG=1	9	8	17
ECOG=2	3	2	5
ECOG=3	1	1	2

End points

End points reporting groups

Reporting group title	Arm A
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Reporting group description:

Obinutuzumab single agent.

Patients received obinutuzumab as a flat dose of 1000 mg on day 1 of each of four 28-day cycles and on days 8 and 15 of cycle 1. Patients with at least a stable disease received obinutuzumab as a flat dose of 1000 mg at weeks 21, 29, 37 and 45.

Reporting group title	Arm B
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Reporting group description:

Obinutuzumab plus Bendamustine.

Patients received obinutuzumab as a flat dose of 1000 mg on day 1 of each of four 28-day cycles and on days 8 and 15 of cycle 1. Additionally, they received bendamustine at a dose of 70 mg/m² by intravenous infusion on days 1 and 2 of each of four 28-day cycles. Patients with at least a stable disease received obinutuzumab as a flat dose of 1000 mg at weeks 21, 29, 37 and 45.

Primary: Overall response rate (ORR)

End point title	Overall response rate (ORR)
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End point description:

Overall response is defined as complete or partial response at the end of the initial treatment phase (after 19-21 weeks).

End point type	Primary
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End point timeframe:

End of the initial treatment phase (after 19-21 weeks)

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	23		
Units: subjects				
overall response = yes	17	22		
overall response = no	6	1		

Statistical analyses

Statistical analysis title	Evaluation of primary outcome in arm A
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Statistical analysis description:

A one-sided binomial test was used to test if the overall response rate in arm A was significantly higher than the pre-specified value of 61%. No statistical comparison between treatment arms A and B was performed. The binomial test was conducted within each treatment arm separately.

Comparison groups	Arm A v Arm B
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Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.14
Method	one-sided binomial test
Parameter estimate	rate
Point estimate	0.739
Confidence interval	
level	95 %
sides	1-sided
lower limit	0.55

Statistical analysis title	Evaluation of primary outcome in arm B
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Statistical analysis description:

A one-sided binomial test was used to test if the overall response rate in arm B was significantly higher than the pre-specified value of 61%. No statistical comparison between treatment arms A and B was performed. The binomial test was conducted within each treatment arm separately.

Comparison groups	Arm A v Arm B
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.00018
Method	one-sided binomial test
Parameter estimate	rate
Point estimate	0.957
Confidence interval	
level	95 %
sides	1-sided
lower limit	0.81

Secondary: 1-year progression-free survival

End point title	1-year progression-free survival
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End point description:

1-year progression-free survival as estimated by the Kaplan-Meier method

End point type	Secondary
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End point timeframe:

From registration to one year after registration

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	23		
Units: subjects				
number (confidence interval 95%)	69.6 (53.1 to 91.2)	87.0 (74.2 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: 2-year progression-free survival

End point title	2-year progression-free survival
End point description:	Two-year progression-free survival as estimated by the Kaplan-Meier method
End point type	Secondary
End point timeframe:	From registration to two years after registration.

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	23		
Units: subjects				
number (confidence interval 95%)	65.2 (48.4 to 87.9)	78.0 (62.7 to 97.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: 1-year overall survival

End point title	1-year overall survival
End point description:	One-year overall survival as estimated by the Kaplan-Meier method
End point type	Secondary
End point timeframe:	From registration to one year after registration

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	23		
Units: subjects				
number (confidence interval 95%)	100 (85.2 to 100)	91.3 (80.5 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: 2-year overall survival

End point title	2-year overall survival
End point description:	Two-year overall survival as estimated by the Kaplan-Meier method
End point type	Secondary
End point timeframe:	From registration to two years after registration

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	23		
Units: subjects				
number (confidence interval 95%)	86.5 (73.4 to 100)	87.0 (74.2 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: 1-year time to treatment failure

End point title	1-year time to treatment failure
End point description:	1-year time to treatment failure as estimated by the Kaplan-Meier method
End point type	Secondary
End point timeframe:	From registration to one year after registration

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	23		
Units: subjects				
number (confidence interval 95%)	65.2 (48.4 to 87.9)	87.0 (74.2 to 100)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From registration to end of study

Adverse event reporting additional description:

There were 166 adverse events in total, 77 of grade 1, 58 of grade 2, 22 of grade 3, 7 of grade 4 and 2 of grade 5.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	4.03
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Reporting groups

Reporting group title	Arm A
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Reporting group description:

All patients that started treatment in arm A

Reporting group title	Arm B
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Reporting group description:

All patients who started treatment in arm B.

Serious adverse events	Arm A	Arm B	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 23 (39.13%)	9 / 23 (39.13%)	
number of deaths (all causes)	4	4	
number of deaths resulting from adverse events	1	1	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder neoplasm			
subjects affected / exposed	0 / 23 (0.00%)	1 / 23 (4.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangiocarcinoma			
subjects affected / exposed	0 / 23 (0.00%)	1 / 23 (4.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clear cell renal cell carcinoma			
subjects affected / exposed	1 / 23 (4.35%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatocellular carcinoma			

subjects affected / exposed	1 / 23 (4.35%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Renal cell carcinoma			
subjects affected / exposed	1 / 23 (4.35%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sarcoma of skin			
subjects affected / exposed	0 / 23 (0.00%)	1 / 23 (4.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 23 (4.35%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid cancer			
subjects affected / exposed	0 / 23 (0.00%)	1 / 23 (4.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Laceration			
subjects affected / exposed	1 / 23 (4.35%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	1 / 23 (4.35%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Peripheral artery aneurysm			
subjects affected / exposed	0 / 23 (0.00%)	1 / 23 (4.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

General disorders and administration site conditions			
Local swelling			
subjects affected / exposed	1 / 23 (4.35%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Rectal haemorrhage			
subjects affected / exposed	1 / 23 (4.35%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	0 / 23 (0.00%)	1 / 23 (4.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 23 (4.35%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 23 (4.35%)	1 / 23 (4.35%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 23 (0.00%)	2 / 23 (8.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
upper respiratory infection			
subjects affected / exposed	0 / 23 (0.00%)	1 / 23 (4.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Tumour lysis syndrome			

subjects affected / exposed	0 / 23 (0.00%)	1 / 23 (4.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Arm A	Arm B	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 23 (73.91%)	21 / 23 (91.30%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			
subjects affected / exposed	0 / 23 (0.00%)	1 / 23 (4.35%)	
occurrences (all)	0	2	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	1 / 23 (4.35%)	2 / 23 (8.70%)	
occurrences (all)	1	2	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 23 (4.35%)	2 / 23 (8.70%)	
occurrences (all)	1	2	
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	2 / 23 (8.70%)	0 / 23 (0.00%)	
occurrences (all)	2	0	
Headache			
subjects affected / exposed	3 / 23 (13.04%)	1 / 23 (4.35%)	
occurrences (all)	3	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 23 (8.70%)	2 / 23 (8.70%)	
occurrences (all)	2	4	
Neutropenia			
subjects affected / exposed	1 / 23 (4.35%)	4 / 23 (17.39%)	
occurrences (all)	2	7	
Thrombocytopenia			

subjects affected / exposed occurrences (all)	4 / 23 (17.39%) 5	2 / 23 (8.70%) 2	
General disorders and administration site conditions			
Chills			
subjects affected / exposed	0 / 23 (0.00%)	2 / 23 (8.70%)	
occurrences (all)	0	3	
Oedema limbs			
subjects affected / exposed	2 / 23 (8.70%)	0 / 23 (0.00%)	
occurrences (all)	2	0	
Fatigue			
subjects affected / exposed	4 / 23 (17.39%)	2 / 23 (8.70%)	
occurrences (all)	4	2	
Fever			
subjects affected / exposed	1 / 23 (4.35%)	2 / 23 (8.70%)	
occurrences (all)	1	2	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 23 (4.35%)	3 / 23 (13.04%)	
occurrences (all)	1	4	
Diarrhoea			
subjects affected / exposed	2 / 23 (8.70%)	1 / 23 (4.35%)	
occurrences (all)	2	1	
Flatulence			
subjects affected / exposed	1 / 23 (4.35%)	1 / 23 (4.35%)	
occurrences (all)	1	1	
Nausea			
subjects affected / exposed	2 / 23 (8.70%)	5 / 23 (21.74%)	
occurrences (all)	2	5	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	4 / 23 (17.39%)	0 / 23 (0.00%)	
occurrences (all)	5	0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 23 (4.35%)	3 / 23 (13.04%)	
occurrences (all)	2	3	

Infections and infestations COVID-19 subjects affected / exposed occurrences (all)	1 / 23 (4.35%) 1	1 / 23 (4.35%) 1	
Lung infection subjects affected / exposed occurrences (all)	1 / 23 (4.35%) 1	1 / 23 (4.35%) 1	
Urinary tract infection subjects affected / exposed occurrences (all)	1 / 23 (4.35%) 1	3 / 23 (13.04%) 3	
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	2 / 23 (8.70%) 2	
Hyperuricaemia subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	2 / 23 (8.70%) 2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 August 2017	New RSI Gazyvaro and Levact Editorial changes
16 October 2018	Changes in regard to new RSI Gazyvaro and Levact.
12 August 2019	Changed study design from Phase III to Phase II. Change in inclusion criteria (open for patient aged 60 and above) Implementation of new interim analysis for IRB.
11 December 2020	Changes in regard to new RSI. Changes in the recruitment period.
03 November 2021	Changed follow up period

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported