Clinical trial results:
Therapy of Nodal Follicular Non-Hodgkin Lymphoma (WHO grade 1/2) in Clinical Stage I/II using Response Adapted Involved Site Radiotherapy in Combination with Gazyvaro

Summary

EudraCT number	2016-002059-89
Trial protocol	DE
Global end of trial date	14 April 2024

Results information

Result version number	v1 (current)
This version publication date	03 May 2026
First version publication date	03 May 2026

Trial information

Trial identification

Sponsor protocol code	GAZAI

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03341520
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University Hospital Heidelberg
Sponsor organisation address	Im Neuenheimer Feld 672, Heidelberg, Germany, 69120
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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	28 July 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 April 2024
Global end of trial reached?	Yes
Global end of trial date	14 April 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The rate of metabolic CR after low-dose radiotherapy in combination with Gazyvaro (Obinutuzumab) for early stage nodal follicular lymphoma was assessed. In addition, the feasibility of a response adapted approach using FDG-PET/CT regarding success (PFS, rates of remission, analysis of recurrences) and safety in combination with Gazyvaro were assessed.
The results were historically compared to the results of the MIR trial regarding morphologic response in week 7 and the quality of life (secondary endpoints). Additional secondary endpoints were PFS, the site of recurrences in the three subgroups (1. PET negative after initial staging; 2. PET negative in week 18; 3. PET positive in week 18).

Primary
Evaluation of the rate of metabolic CR after low-dose involved site radiotherapy in combination with Gazyvaro (Obinutuzumab) in early stage nodal follicular lymphoma in order to avoid conventional full dose IF radiotherapy.

Protection of trial subjects:

Monitoring of all patients for occurrence of adverse events including lab results

Background therapy:

Salvage radiotherapy if there is no metabolical CR and morphological PR/CR/CRu at week 18: additional 18 x 2 Gy (5x2 Gy/week) starting from week 20 (without Obinutuzumab) Dosing according to ICRU 50

Evidence for comparator: -

Actual start date of recruitment	01 April 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: 89
Worldwide total number of subjects	89
EEA total number of subjects	89

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)	67
From 65 to 84 years	22
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

89 patients were recruited.
Eleven patients were excluded due to different stage after PET scan (n=7) , different histology after central pathology review (n=2), extra-nodal disease (n=1) and start of a different therapy (n=1).

Pre-assignment

Screening details:

There was a two stage screening: a) Histology and CT or MRI: centrally approved follicular lymphoma grade 1/2 in clinical stage I/II (max. 93
patients)
b) FDG-PET/CT: exclusion of stage III/IV patients (approx.. 15%= 14 patients) Inclusion of max 79 patients: ca. 70% (=55 patients with remaining lymphoma)

Period 1

Period 1 title	Screening
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

This was a single-arm study.

Arms

Arm title	Screening (no intervention yet)

Arm description: -

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Screening (no intervention yet)
Started	89
Treatment started	89
Completed	78
Not completed	11
different histology after central review	2
extranodal disease	1
start of different therapy	1
different stage after PET scan	7

Period 2

Period 2 title	Full analysis set
Is this the baseline period?	Yes[1]
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

No blinding (single arm study)

Arms

Arm title	Obinutuzumab treatment

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Obinutuzumab
Investigational medicinal product code	L01XC15
Other name	Gazyvaro
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cycle 1, Day 1 (1000 mg): Administer at 50 mg/hr. The rate of the infusion can be escalated in increments of 50 mg/hr every 30 minutes to a maximum rate of 400 mg/hr.
Cycles 2-7: Day 1 (1000 mg). If there were no infusion related side effects during previous administrations, infusions can be started at a rate of 100 mg/hr and increased by 100 mg/hr increments every 30 minutes to a maximum of 400 mg/hr.

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: Period 1 is the screening period. Data regarding age and sex distribution were only available for the full analysis set (period 2)

Number of subjects in period 2[2]	Obinutuzumab treatment
Started	78
Completed	78

Notes:

[2] - 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: Period 1 is the screening period. Data regarding age and sex distribution were only available for the full analysis set (period 2)

Baseline characteristics

Reporting groups

Reporting group title	Full analysis set

Reporting group description: -

Reporting group values	Full analysis set	Total	
Number of subjects	78	78	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	59	59	
From 65-84 years	19	19	
85 years and over	0	0	
Age continuous Units: years			
median	57.0		
full range (min-max)	23.0 to 77.0	-	
Gender categorical Units: Subjects			
Female	41	41	
Male	37	37	

Subject analysis sets

Subject analysis set title	Lymphoma set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The lymphoma set (LS) comprises all patients with initially remaining PET positive lymphoma and consists of 54 patients.

Reporting group values	Lymphoma set		
Number of subjects	54		
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)	40		
From 65-84 years	14		
85 years and over	0		
Age continuous			
Units: years			
median	58		
full range (min-max)	31 to 77		
Gender categorical			
Units: Subjects			
Female	28		
Male	26		

End points

End points reporting groups

Reporting group title	Screening (no intervention yet)
Reporting group description: -	
Reporting group title	Obinutuzumab treatment
Reporting group description: -	
Subject analysis set title	Lymphoma set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The lymphoma set (LS) comprises all patients with initially remaining PET positive lymphoma and consists of 54 patients.

Primary: Metabolic complete response (in week 18 in patients with initially remaining lymphoma judged by FDG PET/CT)

End point title	Metabolic complete response (in week 18 in patients with initially remaining lymphoma judged by FDG PET/CT)[1]

End point description:

Evaluation of the rate of metabolic CR after low dose involved site radiotherapy in combination with Gazyvaro (in early stage nodal follicular lymphoma in order to avoid conventional full dose IF radiotherapy).

End point type	Primary

End point timeframe:

week 18

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: no control arm

End point values	Lymphoma set			
Subject group type	Subject analysis set			
Number of subjects analysed				
Units: number of patients	53			

Attachments (see zip file)	Complete Remission/GAZAI_TableCompleteRemission.png

Statistical analyses

No statistical analyses for this end point

Secondary: Morphologic CR, PR, SD, PD in patients with initially remaining lymphoma judged by CT/MRI, week 7

End point title	Morphologic CR, PR, SD, PD in patients with initially remaining lymphoma judged by CT/MRI, week 7

End point description:

End point type	Secondary

End point timeframe:

week 7

End point values	Lymphoma set			
Subject group type	Subject analysis set			
Number of subjects analysed	54			
Units: number of patients				
Complete Remission	21			
Partial Remission	18			
Stable Disease	15			
Progressive Disease	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Morphologic CR, PR, SD, PD in patients with initially remaining lymphoma judged by CT/MRI, Week 18

End point title	Morphologic CR, PR, SD, PD in patients with initially remaining lymphoma judged by CT/MRI, Week 18

End point description:

End point type	Secondary

End point timeframe:

week 18

End point values	Lymphoma set			
Subject group type	Subject analysis set			
Number of subjects analysed	54			
Units: number of patients				
Complete Remission	49			
Partial Remission	4			
Stable Disease	0			
Progressive Disease	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival: two-year survival rate

End point title	Progression free survival: two-year survival rate

End point description:

End point type	Secondary

End point timeframe:

2 years after individual treatment start

End point values	Lymphoma set			
Subject group type	Subject analysis set			
Number of subjects analysed	54			
Units: survival rate	48			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival: two-year survival rate

End point title	Overall survival: two-year survival rate

End point description:

End point type	Secondary

End point timeframe:

2 year survival following individual treatment start

End point values	Obinutuzumab treatment			
Subject group type	Reporting group			
Number of subjects analysed	78			
Units: survival rate	76			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The observation period begins with the first administration of the Gazyvaro (before the first administration of the Gazyvaro: medical history) and ends with the last study visit, i.e. 30 month after the last take of study medication.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27

Reporting groups

Reporting group title	Full analysis set

Reporting group description: -

Serious adverse events	Full analysis set		
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 78 (11.54%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	0		
Investigations			
Glomerular filtration rate decreased			
subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Non-small cell lung cancer			
subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Transitional cell carcinoma			

subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Lithotripsy			
subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Focal dyscognitive seizures			
subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Middle lobe syndrome			

subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Ureteric obstruction				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary retention				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Cellulitis				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
COVID-19 pneumonia				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	1 / 78 (1.28%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia haemophilus				

subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Full analysis set		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	65 / 78 (83.33%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 78 (6.41%)		
occurrences (all)	6		
Vascular disorders, all other AEs from this SOC			
subjects affected / exposed	8 / 78 (10.26%)		
occurrences (all)	8		
Surgical and medical procedures			
Surgical and medical procedures, all AEs from this SOC			
subjects affected / exposed	5 / 78 (6.41%)		
occurrences (all)	5		
General disorders and administration site conditions			
Eye disorders, all AEs fron this SOC			
subjects affected / exposed	4 / 78 (5.13%)		
occurrences (all)	4		
Fatigue			
subjects affected / exposed	23 / 78 (29.49%)		
occurrences (all)	25		
Pyrexia			
subjects affected / exposed	15 / 78 (19.23%)		
occurrences (all)	15		
Chills			

subjects affected / exposed	6 / 78 (7.69%)		
occurrences (all)	7		
General disorders and administration site conditions, all other AEs from this SOC			
subjects affected / exposed	13 / 78 (16.67%)		
occurrences (all)	15		
Immune system disorders			
Immune system disorders, all AEs from this SOC			
subjects affected / exposed	5 / 78 (6.41%)		
occurrences (all)	5		
Reproductive system and breast disorders			
Gynaecomastia			
subjects affected / exposed	1 / 78 (1.28%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 78 (3.85%)		
occurrences (all)	4		
Respiratory, thoracic and mediastinal disorders, all other AEs from this SOC			
subjects affected / exposed	20 / 78 (25.64%)		
occurrences (all)	22		
Psychiatric disorders			
Psychiatric disorders, all AEs from this SOC			
subjects affected / exposed	7 / 78 (8.97%)		
occurrences (all)	7		
Investigations			
Investigations, all AEs from this SOC			
subjects affected / exposed	18 / 78 (23.08%)		
occurrences (all)	18		
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	11 / 78 (14.10%)		
occurrences (all)	13		
Rib fracture			

subjects affected / exposed	4 / 78 (5.13%)		
occurrences (all)	4		
Injury, poisoning and procedural complications, all other AEs from this SOC			
subjects affected / exposed	7 / 78 (8.97%)		
occurrences (all)	8		
Cardiac disorders			
Cardiac disorders, all AEs from this SOC			
subjects affected / exposed	2 / 78 (2.56%)		
occurrences (all)	2		
Nervous system disorders			
Headache			
subjects affected / exposed	10 / 78 (12.82%)		
occurrences (all)	11		
Nervous system disorders, all other AEs from this SOC			
subjects affected / exposed	21 / 78 (26.92%)		
occurrences (all)	21		
Blood and lymphatic system disorders			
Blood and lymphatic system disorders, all AEs from this SOC			
subjects affected / exposed	7 / 78 (8.97%)		
occurrences (all)	12		
Ear and labyrinth disorders			
Block vertebra			
subjects affected / exposed	1 / 78 (1.28%)		
occurrences (all)	1		
Ear and labyrith disorder, all AEs from this SOC			
subjects affected / exposed	2 / 78 (2.56%)		
occurrences (all)	2		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	5 / 78 (6.41%)		
occurrences (all)	6		
Diarrhoea			
subjects affected / exposed	9 / 78 (11.54%)		
occurrences (all)	10		

Nausea			
subjects affected / exposed	10 / 78 (12.82%)		
occurrences (all)	15		
Gastrointestinal disorders, all other AEs from this SOC			
subjects affected / exposed	20 / 78 (25.64%)		
occurrences (all)	21		
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	1 / 78 (1.28%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Night sweats			
subjects affected / exposed	5 / 78 (6.41%)		
occurrences (all)	6		
Pruritus			
subjects affected / exposed	3 / 78 (3.85%)		
occurrences (all)	4		
Rash			
subjects affected / exposed	3 / 78 (3.85%)		
occurrences (all)	4		
Skin and subcutaneous tissue disorders, all other AEs from this SOC			
subjects affected / exposed	19 / 78 (24.36%)		
occurrences (all)	19		
Renal and urinary disorders			
Renal and urinary disorders, all AEs from this SOC			
subjects affected / exposed	5 / 78 (6.41%)		
occurrences (all)	5		
Endocrine disorders			
Endocrine disorders, all AEs from this SOC			
subjects affected / exposed	2 / 78 (2.56%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Arthralgia			

subjects affected / exposed	7 / 78 (8.97%)		
occurrences (all)	7		
Back pain			
subjects affected / exposed	3 / 78 (3.85%)		
occurrences (all)	4		
Musculoskeletal and connective tissue disorders, all other AEs from this SOC			
subjects affected / exposed	29 / 78 (37.18%)		
occurrences (all)	30		
Infections and infestations			
COVID-19			
subjects affected / exposed	14 / 78 (17.95%)		
occurrences (all)	15		
Urinary tract infection			
subjects affected / exposed	4 / 78 (5.13%)		
occurrences (all)	6		
Nasopharyngitis			
subjects affected / exposed	6 / 78 (7.69%)		
occurrences (all)	7		
Infections and infestations, all other AEs from this SOC			
subjects affected / exposed	31 / 78 (39.74%)		
occurrences (all)	33		
Metabolism and nutrition disorders			
Metabolism and nutrition disorders, all AEs from this SOC			
subjects affected / exposed	9 / 78 (11.54%)		
occurrences (all)	10		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 June 2018	Protocol: adjustment of in --/exclusion criterias (laboratory values); addition of pregnancy test in the follow up phase; regulatory adjustments (adjustme nt of known side effects
06 July 2018	Implementation of notes from the EC
02 January 2019	Protocol: New member of the data monitoring committee; adjustment of milestones; adjustment of second assessor; regulatory adjustments

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported