Clinical trial results:
Phase II study to evaluate the efficacy of upfront obinutuzumab in mantle cell lymphoma patients treated by DHAP followed by autologous transplantation plus obinutuzumab maintenance then MRD driven maintenance

Summary

EudraCT number	2016-000548-33
Trial protocol	FR
Global end of trial date	02 December 2024

Results information

Result version number	v1 (current)
This version publication date	08 April 2026
First version publication date	08 April 2026
Summary attachment (see zip file)	synopsis_Protocol V5.0 (LYMA101_Synopsis Protocol V5.0_EN.pdf)

Trial information

Trial identification

Sponsor protocol code	LyMa101

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02896582
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	LYSARC
Sponsor organisation address	Centre Hospitalier Lyon-Sud Bâtiment 2D, PIERRE-BÉNITE Cedex, France, 69495
Public contact	Project Management , LYSARC, lyma101@lysarc.org
Scientific contact	Pr. Steven Le Gouill , LYSA, steven.legouill@curie.fr

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 December 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 December 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of upfront Obinutuzumab (GA101) at the molecular level (MRD) in bone marrow after induction in patients with previously untreated MCL treated by DHAP.

Protection of trial subjects:

Obinutuzumab must be administered in a clinical (inpatient or outpatient) setting. Full emergency resuscitation facilities should be immediately available and patients should be under close supervision of the investigator at all times
Obinutuzumab should be administered as a slow IV infusion through a dedicated line and after premedications.
The infusion rate of the first GA101 administration is up by 50 mg/hour every thirty minutes until 400 mg/hour to manage potential infusion related reactions or hypersensitivity reactions. For patients who are considered to be at risk of tumor lysis syndrome (TLS) with a high lymphocyte count or bulky lymphoadenopathy, the infusion have to be given extremely slowly (25 mg/hour) over a long period of time or the dose may be split
and given over more than one day. The first recommended dosage is 100 mg followed by 900mg administered on day 1 or day 2. All patients considered at risk should be carefully monitored during the initial days of treatment with a special focus on renal function, potassium, and uric acid values.
The therapy with anti-CD 20 antibodies (obinutuzumab) should be discontinued during the investigations of a
potential PML (Progressive Multifocal Leukoencephalopathy) and permanently stopped if the diagnosis of PML is confirmed. Discontinuation or reduction of any concomitant chemotherapy or immunosuppressive therapy should also be considered
As supportive cares:
G-CSF administration is required during treatment cycles and stem cell collections.
Platelet and red blood cell transfusions are permitted, as necessary.
The use of antibiotics and other supportive therapies is in the discretion of the treating physician.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 September 2016
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	France: 86
Worldwide total number of subjects	86
EEA total number of subjects	86

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)	86
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All 86 patients included in the study were enrolled in France between November 2016 and 02 May 2018.

Pre-assignment

Screening details:

Number of patients screened : 88
Number of patients enrolled : 86

Period 1

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

Arms

Arm title	GA101

Arm description:

Patients receive 4 cycles of GA-DHAP every 21 days and patients at least in stable disease after induction are transplanted.
After ASCT, patients at least in stable disease receive a maintenance : Obinutuzumab every 2 months for 3 years.
The patients with an informative MRD at baseline will continue with 3 additional years of maintenance in wich the patients will receive Obinutuzumab according to their MRD status.

Arm type	Experimental
Investigational medicinal product name	Obinutuzumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

Patients will receive their first Obinutuzumab infusion (1000 mg) on Day 1 (Cycle 1 Day 1) along with standard premedication. During Cycle 1, Obinutuzumab will also be administered on Days 8 and 15.
Cycle 2 to 4: one administration (1000 mg) every 21 days.
Maintenance : 1000 mg every 2 months.

Number of subjects in period 1	GA101
Started	86
Completed	45
Not completed	41
Consent withdrawn by subject	1
Physician decision	2
PATIENT CANNOT BE ON SITE AT EVERY VISIT (COVID19)	1
Adverse event, non-fatal	25
Death	2

NON-RECOVERY OF GA101 WHILE MRD +	1
DELAY BEFORE ASCT TOO LONG	1
MYELODYSPLASIC SYNDROME	1
NON COMPLIANCE WITH STUDY VISITS	1
Protocol deviation	1
Lack of efficacy	5

Baseline characteristics

Reporting groups	
Reporting group title	Treatment (overall period)

Reporting group description: -

Reporting group values	Treatment (overall period)	Total	
Number of subjects	86	86	
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			
median	58		
full range (min-max)	32 to 65	-	
Gender categorical Units: Subjects			
Female	23	23	
Male	63	63	
Ann Arbor stage Units: Subjects			
II	2	2	
III	6	6	
IV	78	78	
MIPI Units: Subjects			
Low risk	47	47	
Intermediate risk	24	24	
High risk	14	14	
Missing	1	1	
Bone Marrow biopsy Units: Subjects			
Involved	54	54	
Not involved	17	17	
Unspecified	4	4	
Missing	11	11	
ECOG Units: Subjects			
_0	55	55	

_1	27	27	
_2	4	4	
Informative MRD Units: Subjects			
Positive >= 10-4	73	73	
Positive <10-4	0	0	
Negative	0	0	
Missing	13	13	

End points

End points reporting groups

Reporting group title	GA101

Reporting group description:

Patients receive 4 cycles of GA-DHAP every 21 days and patients at least in stable disease after induction are transplanted.
After ASCT, patients at least in stable disease receive a maintenance : Obinutuzumab every 2 months for 3 years.
The patients with an informative MRD at baseline will continue with 3 additional years of maintenance in wich the patients will receive Obinutuzumab according to their MRD status.

Subject analysis set title	Efficacy set
Subject analysis set type	Full analysis

Subject analysis set description:

The Efficacy set included all patients having signed the informed consent, received at least one dose of the IMP study drug (Obinutuzumab) and with an informative MRD in BM and/or blood at baseline.

Subject analysis set title	Modified Efficacy set
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The modified Efficacy Set included all patients having signed the informed consent, received at least one dose of the IMP study drug (Obinutuzumab), with an informative MRD in BM and/or blood at baseline and an informative MRD in BM after the 4 cycles of GA-DHAP or at treatment discontinuation.

Primary: MRD negativity (Q-PCR)

End point title	MRD negativity (Q-PCR)[1]

End point description:

MRD negativity rate on Bone Marrow after induction or at treatment discontinuation.

End point type	Primary

End point timeframe:

End of induction

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: The Lyma101 trial was designed in order to detect an increase of 15% of the MRD negativity in bone marrow (BM) rate for patients treated with GA-DHAP, assuming a 80% power at a 5% (1-sided) significance level using a single-stage phase II design.
Experimental treatment will be considered ineffective if the MRD negativity proportion is ≤ 55% (P0) and effective if the MRD negativity proportion ≥ 70% (P1).

End point values	Efficacy set	Modified Efficacy set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	73	68		
Units: percent				
number (confidence interval 95%)				
Negative	75.3 (63.9 to 84.7)	80.9 (69.5 to 89.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: PFS	
End point title	PFS
End point description: The Median-PFS was not reached at the end of study.	
End point type	Secondary
End point timeframe: Since inclusion	

End point values	Efficacy set			
Subject group type	Subject analysis set			
Number of subjects analysed	73			
Units: percent				
number (not applicable)	0			

Attachments (see zip file)	Lyma101 - PFS.jpg

Statistical analyses

No statistical analyses for this end point

Secondary: OS	
End point title	OS
End point description: The Median-OS was not reached at the end of study.	
End point type	Secondary
End point timeframe: Since inclusion	

End point values	Efficacy set			
Subject group type	Subject analysis set			
Number of subjects analysed	73			
Units: percent				
number (not applicable)	0			

Attachments (see zip file)	Lyma101 - OS.jpg

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response rate

End point title	Overall Response rate

End point description:

End point type	Secondary

End point timeframe:

End of Treatment

End point values	Efficacy set			
Subject group type	Subject analysis set			
Number of subjects analysed	73			
Units: percent				
number (confidence interval 95%)	74 (62.4 to 83.6)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs of grade 3-5 for toxicities regardless relationship to investigational product occurring from the date of informed consent signature to 28 day after the last study drug administration of the study will be recorded.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Safety set

Reporting group description:

The Safety set will include all patients having signed the informed consent and received at least one dose of the IMP study drug (Obinutuzumab).

Serious adverse events	Safety set		
Total subjects affected by serious adverse events			
subjects affected / exposed	62 / 85 (72.94%)		
number of deaths (all causes)	15		
number of deaths resulting from adverse events	2		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)			
subjects affected / exposed	7 / 85 (8.24%)		
occurrences causally related to treatment / all	1 / 7		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
VASCULAR DISORDERS			
subjects affected / exposed	2 / 85 (2.35%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS			
subjects affected / exposed	8 / 85 (9.41%)		
occurrences causally related to treatment / all	4 / 9		
deaths causally related to treatment / all	0 / 0		

Immune system disorders IMMUNE SYSTEM DISORDERS			
subjects affected / exposed	2 / 85 (2.35%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS			
subjects affected / exposed	7 / 85 (8.24%)		
occurrences causally related to treatment / all	4 / 8		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders PSYCHIATRIC DISORDERS			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations INVESTIGATIONS			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications INJURY, POISONING AND PROCEDURAL COMPLICATIONS			
subjects affected / exposed	2 / 85 (2.35%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders CARDIAC DISORDERS			
subjects affected / exposed	3 / 85 (3.53%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Nervous system disorders NERVOUS SYSTEM DISORDERS			

subjects affected / exposed	2 / 85 (2.35%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
BLOOD AND LYMPHATIC SYSTEM DISORDERS			
subjects affected / exposed	17 / 85 (20.00%)		
occurrences causally related to treatment / all	23 / 23		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
EYE DISORDERS			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
GASTROINTESTINAL DISORDERS			
subjects affected / exposed	10 / 85 (11.76%)		
occurrences causally related to treatment / all	9 / 12		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
HEPATOBILIARY DISORDERS			
subjects affected / exposed	2 / 85 (2.35%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
RENAL AND URINARY DISORDERS			
subjects affected / exposed	3 / 85 (3.53%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
INFECTIONS AND INFESTATIONS			
subjects affected / exposed	35 / 85 (41.18%)		
occurrences causally related to treatment / all	34 / 51		
deaths causally related to treatment / all	1 / 1		
Metabolism and nutrition disorders			
METABOLISM AND NUTRITION DISORDERS			

subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Safety set		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	82 / 85 (96.47%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)			
subjects affected / exposed	7 / 85 (8.24%)		
occurrences (all)	7		
Vascular disorders			
VASCULAR DISORDERS			
subjects affected / exposed	3 / 85 (3.53%)		
occurrences (all)	3		
General disorders and administration site conditions			
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS			
subjects affected / exposed	10 / 85 (11.76%)		
occurrences (all)	13		
Immune system disorders			
IMMUNE SYSTEM DISORDERS			
subjects affected / exposed	3 / 85 (3.53%)		
occurrences (all)	4		
Respiratory, thoracic and mediastinal disorders			
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS			
subjects affected / exposed	12 / 85 (14.12%)		
occurrences (all)	13		
Psychiatric disorders			
PSYCHIATRIC DISORDERS			
subjects affected / exposed	4 / 85 (4.71%)		
occurrences (all)	4		
Investigations			

INVESTIGATIONS subjects affected / exposed occurrences (all)	 40 / 85 (47.06%) 260		
Injury, poisoning and procedural complications INJURY, POISONING AND PROCEDURAL COMPLICATIONS subjects affected / exposed occurrences (all)	 4 / 85 (4.71%) 4		
Cardiac disorders CARDIAC DISORDERS subjects affected / exposed occurrences (all)	 5 / 85 (5.88%) 5		
Nervous system disorders NERVOUS SYSTEM DISORDERS subjects affected / exposed occurrences (all)	 5 / 85 (5.88%) 5		
Blood and lymphatic system disorders BLOOD AND LYMPHATIC SYSTEM DISORDERS subjects affected / exposed occurrences (all)	 69 / 85 (81.18%) 363		
Ear and labyrinth disorders EAR AND LABYRINTH DISORDERS subjects affected / exposed occurrences (all)	 1 / 85 (1.18%) 1		
Eye disorders EYE DISORDERS subjects affected / exposed occurrences (all)	 1 / 85 (1.18%) 1		
Gastrointestinal disorders GASTROINTESTINAL DISORDERS subjects affected / exposed occurrences (all)	 40 / 85 (47.06%) 66		
Hepatobiliary disorders HEPATOBILIARY DISORDERS subjects affected / exposed occurrences (all)	 7 / 85 (8.24%) 9		
Skin and subcutaneous tissue disorders			

SKIN AND SUBCUTANEOUS TISSUE DISORDERS subjects affected / exposed occurrences (all)	 3 / 85 (3.53%) 3		
Renal and urinary disorders RENAL AND URINARY DISORDERS subjects affected / exposed occurrences (all)	 5 / 85 (5.88%) 5		
Infections and infestations INFECTIONS AND INFESTATIONS subjects affected / exposed occurrences (all)	 50 / 85 (58.82%) 79		
Metabolism and nutrition disorders METABOLISM AND NUTRITION DISORDERS subjects affected / exposed occurrences (all)	 11 / 85 (12.94%) 16		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 October 2016	Protocol v2.0 : Capacity to replace Melphalan by cyclophosphamide
27 February 2017	Protocol v3.0 : - national recommendation to avoid BEAC = suppression of the capacity to use cyclophosphamide instead of Melphalan - recomemndation to treat with COP in case of High risk
14 February 2018	Protocol v4.0 : Bendamustine to replace BCNU Safety declaration rules Secondary Statistics anaysis
17 April 2018	Protocol v5.0 : Suspension of DHAOx Prohibition of oxaliplatine

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported