Clinical trial results:
A PHASE II TRIAL EVALUATING COMBINATION OF ATEZOLIZUMAB, WITH VENETOCLAX AND OBINUTUZUMAB FOR RELAPSED/REFRACTORY LYMPHOMAS

Summary

EudraCT number	2016-005061-31
Trial protocol	FR
Global end of trial date	24 August 2022

Results information

Result version number	v1 (current)
This version publication date	25 May 2025
First version publication date	25 May 2025

Trial information

Trial identification

Sponsor protocol code	GATA

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03276468
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	LYSARC
Sponsor organisation address	165 chemin du grand revoyet, pierre-bénite, France, 69495
Public contact	Project Management , LYSARC, +33 472 66 93 33, gata@lysarc.org
Scientific contact	Project Management , LYSARC, +33 472 66 93 33, gata@lysarc.org

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	24 August 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 August 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

to assess the anti-lymphoma activity of an anti-PD-L1 (atezolizumab) associated with a BCL-2 inhibitor (GDC-199, venetoclax) and an anti-CD20 monoclonal antibody (obinutuzumab) in three separate cohorts:
- relapsed/refractory follicular lymphoma (FL) patients
- relapsed/refractory aggressive (DLBCL) lymphoma patients
- relapsed/refractory other indolent lymphoma patients

Protection of trial subjects:

Corrective treatments possible

Background therapy:

Prophylaxis and corrective treatments

Evidence for comparator: -

Actual start date of recruitment	16 October 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	France: 136
Worldwide total number of subjects	136
EEA total number of subjects	136

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)	100
From 65 to 84 years	36

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

58 patients were included in the GATA cohort 1 FL between the 19 February 2018 and the 26 November 2019.
58 patients were included in the GATA cohort 2 DLBCL between the 12 February 2018 and the 14 March 2019.
20 patients were included in the GATA cohort 3 between the 06 December 2018 and the 18 March 2020.

Pre-assignment

Screening details:

Safety run period:
Twelve patients included in cohorts 1 or 2 who achieved 6 weeks (2 cycles) of treatment (4 doses of obinutuzumab, 2
doses of atezolizumab and 5 weeks of venetoclax) or having discontinued treatment were enrolled in their respective
cohort for safety profile. If one of these 12 patients prematurely discontinued at least one o

Period 1

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

Arms

Arm title	Experimental

Arm description:

Obinutuzumab 1000mg only at induction:
Cycle: Day 1, Day 8 and Day 15
and at each Day 1 from cycle 2 to cycle8

Atezolizumab 1200mg at induction and maintenance:
At each Day 2 from Cycle 1 to Cycle 24

Venetoclax at induction and maintenance:
Given continuously from C1D8 to end of cycle 24
800mg/day for DLBCL and FL cohorts
Step-up dose for iNHL cohort (50mg/d to 400mg/d over 4 weeks, then 800mg/d from week 5)

Arm type	Experimental
Investigational medicinal product name	Obinutuzumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Injection

Dosage and administration details:

1000mg IV at induction only:
Cycle 1: Day 1, 8 and 15
then at each Day 1 from cycle 2 to cycle 8

Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for solution for injection
Routes of administration	Infusion

Dosage and administration details:

1200mg IV at each Day 2 from cycle 1 to cycle 24 (induction and maintenance phases)

Investigational medicinal product name	Venetoclax
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Given orally from Cycle 1 day 8 until end of cycle 24 (induction and maintenance phases).
800mg/day for DLBCL and FL cohorts.
For iNHL cohort: From 50mg/d to 400mg/d over 4 weeks, then 800mg/d from week 5

Number of subjects in period 1	Experimental
Started	136
Completed	136

Baseline characteristics

Reporting groups	
Reporting group title	Experimental
Reporting group description:	
Obinutuzumab 1000mg only at induction: Cycle: Day 1, Day 8 and Day 15 and at each Day 1 from cycle 2 to cycle8 Atezolizumab 1200mg at induction and maintenance: At each Day 2 from Cycle 1 to Cycle 24 Venetoclax at induction and maintenance: Given continuously from C1D8 to end of cycle 24 800mg/day for DLBCL and FL cohorts Step-up dose for iNHL cohort (50mg/d to 400mg/d over 4 weeks, then 800mg/d from week 5)	

Reporting group values	Experimental	Total	
Number of subjects	136	136	
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)	100	100	
From 65-84 years	36	36	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	0		
standard deviation	± 136	-	
Gender categorical Units: Subjects			
Female	56	56	
Male	80	80	

Subject analysis sets	
Subject analysis set title	FAS FL cohort
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
The Full Analysis Set (FAS) includes all patients having signed the informed consent and who received at least one dose of obinutuzumab, atezolizumab and venetoclax. The cohort 1 is the FL cohort.	
Subject analysis set title	FAS DLBCL cohort
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
The Full Analysis Set (FAS) includes all patients having signed the informed consent and who received at	

least one dose of obinutuzumab, atezolizumab and venetoclax.
The cohort 2 is the DLBL cohort

Subject analysis set title	FAS iNHL cohort
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The Full Analysis Set (FAS) includes all patients having signed the informed consent and who received at least one dose of obinutuzumab, atezolizumab and venetoclax.
The cohort 3 is the iNHL cohort

Reporting group values	FAS FL cohort	FAS DLBCL cohort	FAS iNHL cohort
Number of subjects	56	55	18
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)	30	20	6
From 65-84 years	26	34	12
85 years and over	0	1	
Age continuous Units: years			
arithmetic mean	62.8	68.1	68.5
standard deviation	± 10.74	± 10.81	± 9.48
Gender categorical Units: Subjects			
Female	19	25	8
Male	37	30	10

End points

End points reporting groups

Reporting group title	Experimental

Reporting group description:

Obinutuzumab 1000mg only at induction:
Cycle: Day 1, Day 8 and Day 15
and at each Day 1 from cycle 2 to cycle8

Atezolizumab 1200mg at induction and maintenance:
At each Day 2 from Cycle 1 to Cycle 24

Venetoclax at induction and maintenance:
Given continuously from C1D8 to end of cycle 24
800mg/day for DLBCL and FL cohorts
Step-up dose for iNHL cohort (50mg/d to 400mg/d over 4 weeks, then 800mg/d from week 5)

Subject analysis set title	FAS FL cohort
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The Full Analysis Set (FAS) includes all patients having signed the informed consent and who received at least one dose of obinutuzumab, atezolizumab and venetoclax.
The cohort 1 is the FL cohort.

Subject analysis set title	FAS DLBCL cohort
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The Full Analysis Set (FAS) includes all patients having signed the informed consent and who received at least one dose of obinutuzumab, atezolizumab and venetoclax.
The cohort 2 is the DLBL cohort

Subject analysis set title	FAS iNHL cohort
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The Full Analysis Set (FAS) includes all patients having signed the informed consent and who received at least one dose of obinutuzumab, atezolizumab and venetoclax.
The cohort 3 is the iNHL cohort

Primary: Overall Response (CR + PR) Rate at End of Induction

End point title	Overall Response (CR + PR) Rate at End of Induction

End point description:

End point type	Primary

End point timeframe:

at End of Induction

End point values	FAS FL cohort	FAS DLBCL cohort	FAS iNHL cohort	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	56	55	18	
Units: percent				
number (confidence interval 90%)				
ORR	53.6 (41.78 to 65.07)	23.6 (14.58 to 34.93)	66.7 (44.6 to 84.37)	

Statistical analyses

Statistical analysis title	OMR and CR at end of induction
Statistical analysis description: end of induction	
Comparison groups	FAS FL cohort v FAS DLBCL cohort v FAS iNHL cohort
Number of subjects included in analysis	129
Analysis specification	Post-hoc
Analysis type	superiority[1]
P-value	= 1 [2]
Method	t-test, 1-sided
Parameter estimate	Risk ratio (RR)
Confidence interval	
level	95 %
sides	1-sided
upper limit	70
Variability estimate	Standard deviation

Notes:

[1] - end of induction

[2] - No

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Immune-related AEs whatever the grade and AEs of grade ≥ 2 for other toxicities regardless relationship to investigational product occurring from the date of informed consent signature to 6 months after Last drug administration of the study for immune-..

Adverse event reporting additional description:

for immune-related AEs and to 28 days after last drug administration of the study (obinutuzumab, atezolizumab or venetoclax) for other toxicities, will be recorded in the AE pages of the eCRF.
During the initial safety analysis, where twelve patients (cohorts 1 & 2) will be enrolled and followed for 6 weeks of treatment, haematological toxicities.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Safety set C1

Reporting group description:

Final Analysis Cohort 1, Safety set
The Safety set includes all patients who received at least one dose of any study drug.

Reporting group title	Safety set C2

Reporting group description:

Final Analysis Cohort 2, Safety set
The Safety set includes all patients who received at least one dose of any study drug.

Reporting group title	Safety set C3

Reporting group description:

Final Analysis Cohort 3, Safety set
The Safety set includes all patients who received at least one dose of any study drug.

Serious adverse events	Safety set C1	Safety set C2	Safety set C3
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 58 (29.31%)	19 / 57 (33.33%)	7 / 20 (35.00%)
number of deaths (all causes)	23	47	9
number of deaths resulting from adverse events	2	0	0
Investigations			
BLOOD ELECTROLYTE ABNORMAL			
subjects affected / exposed	0 / 58 (0.00%)	1 / 57 (1.75%)	0 / 20 (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
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	1 / 58 (1.72%)	0 / 57 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Injection site hypersensitivity			
subjects affected / exposed	0 / 58 (0.00%)	1 / 57 (1.75%)	3 / 20 (15.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	2 / 58 (3.45%)	0 / 57 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	2 / 58 (3.45%)	2 / 57 (3.51%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 58 (1.72%)	2 / 57 (3.51%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Gastrointestinal infection			
subjects affected / exposed	0 / 58 (0.00%)	2 / 57 (3.51%)	0 / 20 (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

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

Non-serious adverse events	Safety set C1	Safety set C2	Safety set C3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	56 / 58 (96.55%)	56 / 57 (98.25%)	19 / 20 (95.00%)
Blood and lymphatic system disorders			
Neutropenia			

subjects affected / exposed	30 / 58 (51.72%)	24 / 57 (42.11%)	13 / 20 (65.00%)
occurrences (all)	78	70	45
Lymphopenia			
subjects affected / exposed	16 / 58 (27.59%)	27 / 57 (47.37%)	3 / 20 (15.00%)
occurrences (all)	28	49	13
Thrombocytopenia			
subjects affected / exposed	14 / 58 (24.14%)	20 / 57 (35.09%)	6 / 20 (30.00%)
occurrences (all)	22	27	13
Anaemia			
subjects affected / exposed	7 / 58 (12.07%)	22 / 57 (38.60%)	6 / 20 (30.00%)
occurrences (all)	8	37	14
Leukopenia			
subjects affected / exposed	11 / 58 (18.97%)	19 / 57 (33.33%)	3 / 20 (15.00%)
occurrences (all)	32	47	10
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	20 / 58 (34.48%)	6 / 57 (10.53%)	6 / 20 (30.00%)
occurrences (all)	22	12	8
Nausea			
subjects affected / exposed	7 / 58 (12.07%)	7 / 57 (12.28%)	3 / 20 (15.00%)
occurrences (all)	7	7	4
Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	19 / 58 (32.76%)	9 / 57 (15.79%)	1 / 20 (5.00%)
occurrences (all)	29	14	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 November 2019	Protocol amendment with change of the AESI list: addition of hemophagocytic lymphohistiocytosis and macrophage activation syndrome

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.

No

Notes: