



Clinical trial results: BLINAtumomab after R-CHOP debulking therapy for patients with Richter Transformation.

Summary

EudraCT number	2018-003483-32
Trial protocol	FR
Global end of trial date	04 October 2022

Results information

Result version number	v1 (current)
This version publication date	27 June 2025
First version publication date	27 June 2025
Summary attachment (see zip file)	summary french (CLL13 BLINART - RESUME FR v4.0 13.04.21.pdf)

Trial information

Trial identification

Sponsor protocol code	FILOCLL13 BLINART
-----------------------	-------------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03931642
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	FILO (French Innovative Leukemia Organization)
Sponsor organisation address	Hôpital Bretonneau, 2 Bd Tonnellé, TOURS, France, 37044
Public contact	David SCHWARTZ, FILO, 33 0247391896, a.fayault@filo-leucemie.org
Scientific contact	Romain GUIEZE, FILO, 0247473798 0247391896, a.fayault@filo-leucemie.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	20 February 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 October 2022
Global end of trial reached?	Yes
Global end of trial date	04 October 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to determine the objective response to one 8-week cycle of blinatumomab following a debulking therapy with R-CHOP in patients with RS.

Protection of trial subjects:

The personal data processing incurred by this clinical trial is covered by a declaration of conformity to MR-001 (Méthodologie de Référence 1), submitted by the FILO to the French Data Protection Agency, the CNIL. The objective of the process is scientific research, and the legal base is the formal consent of patients and healthcare professionals.

Medical data may be sent only to the sponsor and/or the department responsible for data entry, under the responsibility of the sponsor, and possibly to appropriate health care authorities under conditions guaranteeing data protection.

The sponsor and government authorities may request direct access to medical records to check procedures and/or data from the clinical trial, without violating confidentiality and within limits permitted by laws and regulations.

Background therapy:

R-CHOP: 2 cycles:

Rituximab 375 mg/m² IV Day 1;

Cyclophosphamide 750 mg/m² IV Day 1;

Doxorubicin 50 mg/m² IV Day 1;

Vincristine 1.4 mg/m² [capped at 2.0 mg] IV Day 1

Prednisone 60 mg/m² per day PO Day 1-5

Evidence for comparator: -

Actual start date of recruitment	05 July 2019
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: 39
Worldwide total number of subjects	39
EEA total number of subjects	39

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)	16
From 65 to 84 years	23
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Number of screened patients: 45

Number of enrolled patients (enrolled set): 41

Number of treated patients by RCHOP (full analyses set): 39

Number of treated patient by blinatumomab: 25

Date of first inclusion and last inclusion: 05 July 2019 - 19 JULY 2021

Pre-assignment

Screening details:

Confirmed diagnosis of chronic lymphocytic leukemia or small lymphocytic lymphoma according to the revised iwCLL criteria¹⁹ with biopsy proven transformation to diffuse large B-cell lymphoma, consistent with RS according to the 2016 WHO classification.

Pre-assignment period milestones

Number of subjects started	39
Number of subjects completed	39

Period 1

Period 1 title	RCHOP
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	RCHOP
-----------	-------

Arm description:

2 cycles RCHOP:

Rituximab 375 mg/m² IV Day 1; Cyclophosphamide 750 mg/m² IV Day 1;

Doxorubicin 50 mg/m² IV Day 1; Vincristine 1.4 mg/m² [capped at 2.0 mg] IV Day 1 and

Prednisone 60 mg/m² per day PO Day 1-5

Arm type	Experimental
Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Rituximab 375 mg/m² IV Day 1; Cyclophosphamide 750 mg/m² IV Day 1;

Doxorubicin 50 mg/m² IV Day 1; Vincristine 1.4 mg/m² [capped at 2.0 mg] IV Day 1 and

Prednisone 60 mg/m² per day PO Day 1-5

Number of subjects in period 1	RCHOP
Started	39
Evaluation after RCHOP n°2	25
Completed	25
Not completed	14
Adverse event, serious fatal	3
complete response after RCHOP	9
Adverse event, non-fatal	1
Lack of efficacy	1

Period 2

Period 2 title	Blinatumomab induction
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Blinatumomab
-----------	--------------

Arm description:

Patient treated by blinatumomab after 2 cycles of RCHOP

Blinatumomab at 9 µg/d IV by continuous vein infusion from day 1-7 (W8), 28 µg/d from day 8-14 (W9) and 112 µg/d from day 15-56 (W10-15). The total induction cycle is 8 weeks in duration.

Arm type	Experimental
Investigational medicinal product name	blinatumomab
Investigational medicinal product code	J9039
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Blinatumomab at 9 µg/d IV by continuous vein infusion from day 1-7 (W8), 28

µg/d from day 8-14 (W9) and 112 µg/d from day 15-56 (W10-15). The total induction cycle is 8 weeks in duration.

Number of subjects in period 2	Blinatumomab
Started	25
Evaluation after blinatumomab induction	18
Completed	18
Not completed	7
Adverse event, non-fatal	1
Lack of efficacy	6

Baseline characteristics

Reporting groups

Reporting group title	RCHOP
-----------------------	-------

Reporting group description: -

Reporting group values	RCHOP	Total	
Number of subjects	39	39	
Age categorical			
age > 18 years old			
Units: Subjects			
Adults (18-64 years)	16	16	
From 65 to 84 years	23	23	
Gender categorical			
Units: Subjects			
Female	26	26	
Male	13	13	

End points

End points reporting groups

Reporting group title	RCHOP
Reporting group description: 2 cycles RCHOP: Rituximab 375 mg/m ² IV Day 1; Cyclophosphamide 750 mg/m ² IV Day 1; Doxorubicin 50 mg/m ² IV Day 1; Vincristine 1.4 mg/m ² [capped at 2.0 mg] IV Day 1 and Prednisone 60 mg/m ² per day PO Day 1-5	
Reporting group title	Blinatumomab
Reporting group description: Patient treated by blinatumomab after 2 cycles of RCHOP Blinatumomab at 9 µg/d IV by continuous vein infusion from day 1-7 (W8), 28 µg/d from day 8-14 (W9) and 112 µg/d from day 15-56 (W10-15). The total induction cycle is 8 weeks in duration.	

Primary: Evaluation 2

End point title	Evaluation 2 ^[1]
End point description: Response after blinatumomab induction (evaluation 2 W16) CT-scan: done/not done 18/25 (72%) PET: done/not done 17/25 (68%) BOM: done/not done 3/25 (12%) Result: CR : 5/25 (20.0%) PR : 4/25 (16.0%) Stable : 1/25 (4.0%) Not evaluable: 6/25 (24.0%) Progressive disease: 9/25 (36.0%)	
End point type	Primary
End point timeframe: after blinatumomab induction (week 16)	
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: Done but not completed here	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

During blinatumomab treatment

Must be reported and collected in the CRF all the adverse event (any grade) according to the CTCAE system.

AEs will be monitored until they disappear

Adverse event reporting additional description:

During follow up period

All the adverse event (any grade) must continue to be reported to 30 days after the last dose of study treatment.

After only adverse event possibly related to IP must to be reported to the last follow up visit.

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	CTCAE
Dictionary version	5.0

Reporting groups

Reporting group title	during blinatumomab induction therapy.
-----------------------	--

Reporting group description: -

Serious adverse events	during blinatumomab induction therapy.		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 25 (32.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Vascular disorders			
thromboembolic event			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombosis			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Nervous system disorders Encephalopathy	subjects affected / exposed	1 / 25 (4.00%)		
	occurrences causally related to treatment / all	1 / 1		
	deaths causally related to treatment / all	0 / 0		
	tremor	Additional description: ICANS		
	subjects affected / exposed	1 / 25 (4.00%)		
	occurrences causally related to treatment / all	1 / 1		
	deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions	fever			
	subjects affected / exposed	1 / 25 (4.00%)		
	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 / 25 (4.00%)		
	occurrences causally related to treatment / all	1 / 1		
	deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders	gastrointestinal perforation			
	subjects affected / exposed	1 / 25 (4.00%)		
	occurrences causally related to treatment / all	1 / 1		
	deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders	Pulmonary embolism			
	subjects affected / exposed	1 / 25 (4.00%)		
	occurrences causally related to treatment / all	0 / 1		
	deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders	Osteolysis			
	subjects affected / exposed	1 / 25 (4.00%)		
	occurrences causally related to treatment / all	0 / 1		
	deaths causally related to treatment / all	0 / 0		

Infections and infestations Septic shock subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 25 (4.00%) 0 / 1 0 / 0		
catheter infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 25 (4.00%) 0 / 1 0 / 0		
Metabolism and nutrition disorders hyperglycemia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 25 (4.00%) 1 / 1 0 / 0		

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

Non-serious adverse events	during blinatumomab induction therapy.		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 25 (100.00%)		
Investigations			
Lymphocyte count decrease			
subjects affected / exposed	6 / 25 (24.00%)		
occurrences (all)	6		
Hyperglycaemia			
subjects affected / exposed	5 / 25 (20.00%)		
occurrences (all)	5		
White blood cell count decrease			
subjects affected / exposed	4 / 25 (16.00%)		
occurrences (all)	4		
Platelet count decrease			
subjects affected / exposed	4 / 25 (16.00%)		
occurrences (all)	4		
Hypomagnesaemia			

subjects affected / exposed	4 / 25 (16.00%)		
occurrences (all)	4		
Neutrophil count decrease			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	3		
GGT increased			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Alkaline phosphatase increased			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Hyperkalaemia			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Hypokalaemia			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Hypocalcemia			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Hyponatraemia			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Nervous system disorders			
headache			
subjects affected / exposed	4 / 25 (16.00%)		
occurrences (all)	4		
tremors			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Paresthesia			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Confusion			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		

General disorders and administration site conditions			
fever			
subjects affected / exposed	9 / 25 (36.00%)		
occurrences (all)	9		
oedema limb			
subjects affected / exposed	4 / 25 (16.00%)		
occurrences (all)	4		
Fatigue			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
anemia			
subjects affected / exposed	6 / 25 (24.00%)		
occurrences (all)	6		
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	4 / 25 (16.00%)		
occurrences (all)	4		
hypogammaglobulinaemia			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Dyspnea			
subjects affected / exposed	4 / 25 (16.00%)		
occurrences (all)	4		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Infections and infestations			
Sepsis			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
Hypoalbuminaemia			
subjects affected / exposed	4 / 25 (16.00%)		
occurrences (all)	4		

Diarrhea			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	3		
Constipation			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Cholecystitis			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 January 2021	extension of the inclusion period from 18 to 36 months
11 May 2021	addition of 6 patients

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/39122717>