Clinical trial results:
STUDY OF THE EFFICACY AND SAFETY OF FIRST LINE TREATMENT WITH CHOP AND LENALIDOMIDE (Rev-CHOP) IN PATIENTS AGED FROM 60 TO 80 YEARS WITH PREVIOUSLY UNTREATED ANGIOIMMUNOBLASTIC T-CELL LYMPHOMA (AITL).

Summary

EudraCT number	2011-001356-10
Trial protocol	BE
Global end of trial date	21 March 2019

Results information

Result version number	v1 (current)
This version publication date	25 February 2021
First version publication date	25 February 2021

Trial information

Trial identification

Sponsor protocol code	Revail

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	LYSARC
Sponsor organisation address	CH LYON SUD BATIMENT 2D, PIERRE BENITE, France, 69495
Public contact	Project Manager, LYSARC, +33 (0)472669333, revail@lysarc.org
Scientific contact	Project Manager, LYSARC, +33 (0)472669333, revail@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	21 March 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 March 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to evaluate the Complete Metabolic Response (CMR) rate at the end of treatment.

Protection of trial subjects:

patient could receive salvage treatment

Background therapy:

CHOP : cyclophosphamide - prednisone- doxorubicine - vincristine

Evidence for comparator: -

Actual start date of recruitment	28 November 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	France: 77
Worldwide total number of subjects	80
EEA total number of subjects	80

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)	15
From 65 to 84 years	65
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

France: first recruitment: 28NOV2011 and last recruitment: 09MAR2017
Belgium: first recruitment: 25AUG2015 and last recruitment: 14FEB2017

Pre-assignment

Screening details:

no previous therapy; histologically proven T-cell angioimmunoblastic lymphoma (AITL)
80 patients are included

Period 1

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

Arms

Arm title	Experimental

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Lenalidomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

25mg D1 to D4 - 8 cycles of 21 days

Number of subjects in period 1	Experimental
Started	80
Completed	78
Not completed	2
Consent withdrawn by subject	1
rapid change in his/her general condition	1

Period 2

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

Arms

Arm title	Experimental
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Lenalidomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

25mg D1 to D4 - 8 cycles of 21 days

Number of subjects in period 2	Experimental
Started	78
Completed	44
Not completed	34
Adverse event, serious fatal	3
REVLIMID STOPPED (PATIENT DECISION)	1
INVESTIGATOR DECISION (DUE TO STABLE DISEASE)	1
Consent withdrawn by subject	2
PATIENT REFUSED TO FOLLOW THE REVLIMID TREATMENT	1
Adverse event, non-fatal	13
LENALIDOMIDE STOPPED DUE TO HEMATOLOGIC TOXICITY	1
PATIENT FINALLY REFUSED TO BE TREATED WITH REVLIMI	1
PATIENT REFUSAL FOR FURTHER CONTINUATION	1
Lack of efficacy	8
Protocol deviation	2

Baseline characteristics

Reporting groups

Reporting group title	Baseline

Reporting group description: -

Reporting group values	Baseline	Total	
Number of subjects	80	80	
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	69		
inter-quartile range (Q1-Q3)	66 to 72	-	
Gender categorical Units: Subjects			
Female	42	42	
Male	38	38	

Subject analysis sets

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

Subject analysis set description:

The efficacy set includes evaluable patients.
Evaluable patients are defined as all patients who received at least one cycle of Rev-CHOP:
- with complete treatment and with central review of PET scans at baseline and at the end of treatment
- or prematurely withdrawn before C8
This population will be used for all efficacy analyses.

Subject analysis set title	AITL/TFH set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects who received at least one dose of Lenalidomide and one cycle of CHOP and had a confirmed diagnosis of AITL or nodal PTCL with a TFH phenotype. These subjects were included in the sensitivity analysis.

Reporting group values	Efficacy set	AITL/TFH set	
Number of subjects	78	71	
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous Units: years			
median	69		
inter-quartile range (Q1-Q3)	66 to 72		
Gender categorical Units: Subjects			
Female	41		
Male	37		

End points

End points reporting groups

Reporting group title	Experimental
Reporting group description: -	
Reporting group title	Experimental
Reporting group description: -	
Subject analysis set title	Efficacy set
Subject analysis set type	Full analysis

Subject analysis set description:

The efficacy set includes evaluable patients.
Evaluable patients are defined as all patients who received at least one cycle of Rev-CHOP:
- with complete treatment and with central review of PET scans at baseline and at the end of treatment
- or prematurely withdrawn before C8
This population will be used for all efficacy analyses.

Subject analysis set title	AITL/TFH set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects who received at least one dose of Lenalidomide and one cycle of CHOP and had a confirmed diagnosis of AITL or nodal PTCL with a TFH phenotype. These subjects were included in the sensitivity analysis.

Primary: Complete Metabolic Response at end of treatment based on central review

End point title	Complete Metabolic Response at end of treatment based on central review[1]

End point description:

The primary endpoint is the Complete Metabolic Response (CMR) rate at the end of treatment according to Lugano classification and based on PET scan independent central review.
Response are assessed after completion of treatment if all planned cycles were delivered or at withdrawal.

End point type	Primary

End point timeframe:

At end of treatment, i.e. after complete treatment or at treatment discontinuation

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 conclusion of the trial is based on the confidence interval related to the primary criterion. This interval is compared to the proportion of respondors at end of treatmentaccording to the null hypothesis : 0.45.
There is no arm comparison.

End point values	Efficacy set			
Subject group type	Subject analysis set			
Number of subjects analysed	78			
Units: percent				
number (confidence interval 90%)	41.0 (31.6 to 51.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Complete Response (CR) rate according to Cheson 2007 criteria based on investigator evaluation

End point title	Complete Response (CR) rate according to Cheson 2007 criteria based on investigator evaluation

End point description:

Complete Response (CR) rate according to Cheson 2007 criteria based on investigator evaluation of PET scan will be used as secondary endpoint. Patient without response assessment (due to whatever reason) will be considered as non-responder.

End point type	Secondary

End point timeframe:

At end of treatment, i.e. after completed treatment or at premature treatment discontinuation

End point values	Efficacy set			
Subject group type	Subject analysis set			
Number of subjects analysed	78			
Units: percent				
number (confidence interval 95%)	35.9 (25.3 to 47.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS)

End point title	Progression-Free Survival (PFS)

End point description:

Progression-Free Survival (PFS) is measured from the date of inclusion to the date of first documented disease progression, relapse or death from any cause, whichever occurs first.
Responding patients and patients who are lost to follow up are censored at their last tumor assessment date.

End point type	Secondary

End point timeframe:

2-year PFS

End point values	Efficacy set			
Subject group type	Subject analysis set			
Number of subjects analysed	78			
Units: percent				
number (confidence interval 95%)	42.1 (30.9 to 52.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

Overall survival (OS) is measured from the date of inclusion to the date of death from any cause. Patients alive are censored at their last follow-up date. Patients who are alive or lost to follow-up at the time of analysis are censored at the date of the last contact.

End point type	Secondary

End point timeframe:

2-year OS

End point values	Efficacy set			
Subject group type	Subject analysis set			
Number of subjects analysed	78			
Units: percent				
number (confidence interval 95%)	59.2 (47.3 to 69.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Event-Free Survival (EFS)

End point title	Event-Free Survival (EFS)

End point description:

Event-Free survival (EFS) is measured from the date of inclusion to the date of first documented disease progression, relapse, initiation of new anti-lymphoma therapy or death from any cause.
Responding patients and patients who are lost to follow up are censored at their last tumor assessment date.

End point type	Secondary

End point timeframe:

2-year EFS

End point values	Efficacy set			
Subject group type	Subject analysis set			
Number of subjects analysed	78			
Units: percent				
number (confidence interval 95%)	35.5 (25.0 to 46.2)			

Statistical analyses

No statistical analyses for this end point

Post-hoc: Sensitivity analysis of complete Metabolic Response at end of treatment based on central review

End point title	Sensitivity analysis of complete Metabolic Response at end of treatment based on central review

End point description:

Complete Metabolic Response (CMR) rate at the end of treatment according to Lugano classification and based on PET scan independent central review on subject with confirmed diagnosis (AITL/TFH set). Response are assessed after completion of treatment if all planned cycles were delivered or at withdrawal.

End point type	Post-hoc

End point timeframe:

At end of treatment, i.e. after complete treatment or at treatment discontinuation

End point values	AITL/TFH set			
Subject group type	Subject analysis set			
Number of subjects analysed	71			
Units: percent				
number (confidence interval 90%)	42.3 (32.3 to 52.7)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From informed consent up to 30 days after the last study drug

Adverse event reporting additional description:

All adverse events of intensity grade ≥ 2 regardless of relationship to Revlimid that occurred after the informed consent up to 30 days after the last study drug administration are recorded.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	4.03

Reporting groups

Reporting group title	Safety set

Reporting group description:

The safety set includes all patients who have received at least one dose of Revlimid (lenalidomide). The safety set is used for all safety analyses.

Serious adverse events	Safety set		
Total subjects affected by serious adverse events			
subjects affected / exposed	36 / 78 (46.15%)		
number of deaths (all causes)	42		
number of deaths resulting from adverse events	5		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)			
subjects affected / exposed	4 / 78 (5.13%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
VASCULAR DISORDERS			
subjects affected / exposed	3 / 78 (3.85%)		
occurrences causally related to treatment / all	3 / 4		
deaths causally related to treatment / all	1 / 1		
General disorders and administration site conditions			
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS			

subjects affected / exposed	7 / 78 (8.97%)		
occurrences causally related to treatment / all	1 / 8		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS			
subjects affected / exposed	4 / 78 (5.13%)		
occurrences causally related to treatment / all	3 / 4		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
PSYCHIATRIC DISORDERS			
subjects affected / exposed	1 / 78 (1.28%)		
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	1 / 78 (1.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
CARDIAC DISORDERS			
subjects affected / exposed	4 / 78 (5.13%)		
occurrences causally related to treatment / all	2 / 5		
deaths causally related to treatment / all	1 / 1		
Nervous system disorders			
NERVOUS SYSTEM DISORDERS			
subjects affected / exposed	3 / 78 (3.85%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
BLOOD AND LYMPHATIC SYSTEM DISORDERS			
subjects affected / exposed	3 / 78 (3.85%)		
occurrences causally related to treatment / all	3 / 5		
deaths causally related to treatment / all	0 / 1		

Gastrointestinal disorders			
GASTROINTESTINAL DISORDERS			
subjects affected / exposed	5 / 78 (6.41%)		
occurrences causally related to treatment / all	4 / 6		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
SKIN AND SUBCUTANEOUS TISSUE DISORDERS			
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			
RENAL AND URINARY DISORDERS			
subjects affected / exposed	4 / 78 (5.13%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	1 / 1		
Endocrine disorders			
ENDOCRINE DISORDERS			
subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS			
subjects affected / exposed	1 / 78 (1.28%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Infections and infestations			
subjects affected / exposed	21 / 78 (26.92%)		
occurrences causally related to treatment / all	16 / 27		
deaths causally related to treatment / all	3 / 4		
Metabolism and nutrition disorders			
METABOLISM AND NUTRITION DISORDERS			

subjects affected / exposed	5 / 78 (6.41%)		
occurrences causally related to treatment / all	4 / 5		
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	78 / 78 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	Additional description: All AEs from this SOC have been pooled		
subjects affected / exposed	4 / 78 (5.13%)		
occurrences (all)	4		
Vascular disorders			
VASCULAR DISORDERS	Additional description: All AEs from this SOC have been pooled		
subjects affected / exposed	12 / 78 (15.38%)		
occurrences (all)	14		
Surgical and medical procedures			
SURGICAL AND MEDICAL PROCEDURES	Additional description: All AEs from this SOC have been pooled		
subjects affected / exposed	1 / 78 (1.28%)		
occurrences (all)	1		
General disorders and administration site conditions			
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	Additional description: All AEs from this SOC have been pooled		
subjects affected / exposed	34 / 78 (43.59%)		
occurrences (all)	44		
Respiratory, thoracic and mediastinal disorders			
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	Additional description: All AEs from this SOC have been pooled		
subjects affected / exposed	13 / 78 (16.67%)		
occurrences (all)	14		
Psychiatric disorders			
PSYCHIATRIC DISORDERS	Additional description: All AEs from this SOC have been pooled		
subjects affected / exposed	3 / 78 (3.85%)		
occurrences (all)	3		

Investigations			
INVESTIGATIONS	Additional description: All AEs from this SOC have been pooled		
subjects affected / exposed	16 / 78 (20.51%)		
occurrences (all)	20		
Injury, poisoning and procedural complications			
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	Additional description: All AEs from this SOC have been pooled		
subjects affected / exposed	4 / 78 (5.13%)		
occurrences (all)	5		
Congenital, familial and genetic disorders			
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	Additional description: All AEs from this SOC have been pooled		
subjects affected / exposed	2 / 78 (2.56%)		
occurrences (all)	2		
Cardiac disorders			
CARDIAC DISORDERS	Additional description: All AEs from this SOC have been pooled		
subjects affected / exposed	6 / 78 (7.69%)		
occurrences (all)	8		
Nervous system disorders			
NERVOUS SYSTEM DISORDERS	Additional description: All AEs from this SOC have been pooled		
subjects affected / exposed	20 / 78 (25.64%)		
occurrences (all)	23		
Blood and lymphatic system disorders			
BLOOD AND LYMPHATIC SYSTEM DISORDERS	Additional description: All AEs from this SOC have been pooled		
subjects affected / exposed	77 / 78 (98.72%)		
occurrences (all)	1007		
Eye disorders			
EYE DISORDERS	Additional description: All AEs from this SOC have been pooled		
subjects affected / exposed	3 / 78 (3.85%)		
occurrences (all)	3		
Gastrointestinal disorders			
GASTROINTESTINAL DISORDERS	Additional description: All AEs from this SOC have been pooled		
subjects affected / exposed	32 / 78 (41.03%)		
occurrences (all)	53		
Hepatobiliary disorders			
HEPATOBILIARY DISORDERS	Additional description: All AEs from this SOC have been pooled		
subjects affected / exposed	6 / 78 (7.69%)		
occurrences (all)	6		

Skin and subcutaneous tissue disorders			
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	Additional description: All AEs from this SOC have been pooled		
subjects affected / exposed	9 / 78 (11.54%)		
occurrences (all)	10		
Renal and urinary disorders			
RENAL AND URINARY DISORDERS	Additional description: All AEs from this SOC have been pooled		
subjects affected / exposed	9 / 78 (11.54%)		
occurrences (all)	9		
Endocrine disorders			
ENDOCRINE DISORDERS	Additional description: All AEs from this SOC have been pooled		
subjects affected / exposed	1 / 78 (1.28%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	Additional description: All AEs from this SOC have been pooled		
subjects affected / exposed	13 / 78 (16.67%)		
occurrences (all)	16		
Infections and infestations			
INFECTIONS AND INFESTATIONS	Additional description: All AEs from this SOC have been pooled		
subjects affected / exposed	42 / 78 (53.85%)		
occurrences (all)	60		
Metabolism and nutrition disorders			
METABOLISM AND NUTRITION DISORDERS	Additional description: All AEs from this SOC have been pooled		
subjects affected / exposed	18 / 78 (23.08%)		
occurrences (all)	38		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 January 2012	• Precision regarding prophylaxis treatment, that all subjects will be required to take a low molecular weight heparin as thromboembolic event prophylaxis during study period. • Modification of non-inclusion criteria n°9 to add that any history of malignancy, other than that treated in this research, unless the subject has remained free of the disease for over 5 years
20 February 2015	• Modification of the study duration from 42 months to 78 months and date of the end of study due to recruitment slower than expected
18 March 2016	• Modification of the primary objective to become the CMR according to Lugano Classification. • The CRR according to Cheson 2007 becomes a secondary objective. • Adding in appendix of Lugano 2014 criteria • Clarification of the term "withdraw" which means withdraw of study treatment but does not exclude from follow-up period. • Precision on the adverse event and serious adverse event reporting such as adverse events will not recorded after the start of a new chemotherapy treatment or after lymphoma progression, except if considered related to study treatment. • Update of the Lenalidomide Pregnancy Prevention Plan
27 February 2017	• Adding of biological studies • Precision on progression criteria not-based only on CT-Scan, it should be based on CT scan or relevant clinical data, exams (e.g. PET-Scan). • Precision on follow-up period, thus subjects will be followed 18 months after the last subject included has completed the treatment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported