Clinical trial results:
Phase 3 Multi-Center Randomized Study to Compare Efficacy and Safety of Romidepsin¬CHOP (Ro-CHOP) versus CHOP in subjects with Previously Untreated Peripheral T-Cell Lymphoma.

Summary

EudraCT number	2012-001580-68
Trial protocol	BE ES IT DE PT AT
Global end of trial date	13 December 2022

Results information

Result version number	v1 (current)
This version publication date	15 December 2023
First version publication date	15 December 2023
Summary attachment (see zip file)	20190717_Ro-CHOP Study_Synopsis (20190717_Ro-CHOP Study_Synopsis_v5.0.pdf)

Trial information

Trial identification

Sponsor protocol code	Ro-CHOP Study

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	LYSARC
Sponsor organisation address	Centre Hospitalier Lyon-Sud - Bâtiment 2D, PIERRE-BENITE, France, 69495
Public contact	Fabienne MORAND, LYSARC, 33 472 66 93 33, fabienne.morand@lysarc.org
Scientific contact	Fabienne MORAND, LYSARC, 33 472 66 93 33, fabienne.morand@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	13 December 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 December 2022
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 compare efficacy of romidepsin when administered with CHOP versus CHOP alone in subjects with previously untreated peripheral T-cell lymphoma (PTCL)

Protection of trial subjects:

DSMC periodically reviewed the safety and efficacy data from the trial prepared by the independent statistician. All data presented at the meeting were confidential. Following each meeting the DMSC prepared a report and may recommended changes in the trial conduct.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 January 2013
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	Spain: 44
Country: Number of subjects enrolled	Belgium: 34
Country: Number of subjects enrolled	France: 252
Country: Number of subjects enrolled	Germany: 17
Country: Number of subjects enrolled	Italy: 24
Country: Number of subjects enrolled	Korea, Republic of: 22
Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	Singapore: 16
Country: Number of subjects enrolled	Austria: 7
Worldwide total number of subjects	421
EEA total number of subjects	378

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)	202
From 65 to 84 years	219
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

420 planned (210/treatment arm); 421 enrolled; 421 randomized subjects (211 subjects in Ro-CHOP arm and 210 subjects in CHOP arm), and 418 treated (210 subjects in Ro-CHOP arm and 208 subjects in CHOP arm).

Pre-assignment

Screening details:

The study consisted of 3 phases: Screening Phase, Treatment Phase, and Follow-up Phase. Subjects were eligible for screening once they had signed the informed consent form. In the Screening Phase, subjects were to undergo baseline assessments of their disease and other assessments up to 14 days before first dose of study drug, except for imaging

Period 1

Period 1 title	Treatment phase
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Ro-CHOP

Arm description:

Romidepsin + CHOP 6 cycles

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

Dosage and administration details:

Romidepsin was supplied as a dual pack containing 10 mg lyophilized romidepsin and 20 mg povidone in a sterile single-use vial (active drug) and 2 mL of 20% ethanol in propylene glycol in a sterile single use vial (diluent). Romidepsin was reconstituted with the supplied diluent (5 mg/mL solution) and further diluted with 0.9% sodium chloride injection before IV infusion. Romidepsin was administered in Arm B, Ro-CHOP regimen at the dose of 12 mg/m² IV infused over a 4-hour period on Days 1 and 8 of a 21-day cycle.

Arm title	CHOP

Arm description:

CHOP 6 cycles cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP)

Arm type	Active comparator
Investigational medicinal product name	Romidepsin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Injection

Dosage and administration details:

Romidepsin was supplied as a dual pack containing 10 mg lyophilized romidepsin and 20 mg povidone in a sterile single-use vial (active drug) and 2 mL of 20% ethanol in propylene glycol in a sterile single use vial (diluent). Romidepsin was reconstituted with the supplied diluent (5 mg/mL solution) and further diluted with 0.9% sodium chloride injection before IV infusion. Romidepsin was administered in Arm B, Ro-CHOP regimen at the dose of 12 mg/m² IV infused over a 4-hour period on Days 1 and 8 of a 21-day cycle.

Number of subjects in period 1	Ro-CHOP	CHOP
Started	211	210
Completed	164	154
Not completed	47	56
Consent withdrawn by subject	2	4
toxicity	3	4
insufficient response	1	4
Death	2	2
Other	8	7
Progression	28	33
Concurrent illness	3	2

Period 2

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Ro-CHOP

Arm description:

Romidepsin + CHOP 6 cycles

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

Dosage and administration details:

Romidepsin was supplied as a dual pack containing 10 mg lyophilized romidepsin and 20 mg povidone in a sterile single-use vial (active drug) and 2 mL of 20% ethanol in propylene glycol in a sterile single use vial (diluent). Romidepsin was reconstituted with the supplied diluent (5 mg/mL solution) and further diluted with 0.9% sodium chloride injection before IV infusion. Romidepsin was administered in Arm B, Ro-CHOP regimen at the dose of 12 mg/m² IV infused over a 4-hour period on Days 1 and 8 of a 21-day cycle.

Arm title	Standard arm

Arm description:

Cyclophosphamide, doxorubicine, vincristine, and prednisone (CHOP) 6 cycles

Arm type	Active comparator

Investigational medicinal product name	Romidepsin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Injection

Dosage and administration details:

Romidepsin was supplied as a dual pack containing 10 mg lyophilized romidepsin and 20 mg povidone in a sterile single-use vial (active drug) and 2 mL of 20% ethanol in propylene glycol in a sterile single use vial (diluent). Romidepsin was reconstituted with the supplied diluent (5 mg/mL solution) and further diluted with 0.9% sodium chloride injection before IV infusion. Romidepsin was administered in Arm B, Ro-CHOP regimen at the dose of 12 mg/m² IV infused over a 4-hour period on Days 1 and 8 of a 21-day cycle.

Number of subjects in period 2	Ro-CHOP	Standard arm
Started	164	154
Completed	62	59
Not completed	102	95
Consent withdrawn by subject	10	7
Death	75	77
Lost to follow-up	17	11

Baseline characteristics

Reporting groups	
Reporting group title	Ro-CHOP
Reporting group description:	
Romidepsin + CHOP 6 cycles	
Reporting group title	CHOP
Reporting group description:	
CHOP 6 cycles cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP)	

Reporting group values	Ro-CHOP	CHOP	Total
Number of subjects	211	210	421
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			
Age at baseline			
Units: years			
median	65.0	65.0	
full range (min-max)	26 to 80	25 to 81	-
Gender categorical			
Units: Subjects			
Female	86	74	160
Male	125	136	261

End points

End points reporting groups	
Reporting group title	Ro-CHOP
Reporting group description: Romidepsin + CHOP 6 cycles	
Reporting group title	CHOP
Reporting group description: CHOP 6 cycles cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP)	
Reporting group title	Ro-CHOP
Reporting group description: Romidepsin + CHOP 6 cycles	
Reporting group title	Standard arm
Reporting group description: Cyclophosphamide, doxorubicine, vincristine, and prednisone (CHOP) 6 cycles	

Primary: Progression Free Survival	
End point title	Progression Free Survival
End point description:	
End point type	Primary
End point timeframe: Median progression free survival from randomization	

End point values	Ro-CHOP	CHOP		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	211	210		
Units: months				
median (confidence interval 95%)	12.0 (9.0 to 25.8)	10.2 (7.4 to 13.2)		

Attachments (see zip file)	Ro CHOP PFS/Figure 164212.png

Statistical analyses

Statistical analysis title	stratified log-rank test of difference in PFS
Comparison groups	Ro-CHOP v CHOP

Number of subjects included in analysis	421
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0274
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.789
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	1.005

Secondary: Overall Survival

End point title	Overall Survival

End point description:

End point type	Secondary

End point timeframe:

Overall survival from date of randomization

End point values	Ro-CHOP	CHOP		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	211	210		
Units: months				
median (confidence interval 95%)	62.2 (35.7 to 86.6)	43.8 (30.1 to 70.2)		

Attachments (see zip file)	Ro CHOP OS/Figure 172103.png

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

After the subject signed the informed consent until 30 days after the last study drug administration.

Adverse event reporting additional description:

All adverse events (AE), whatever grade of intensity, occurring from the date of informed consent signature until 30 days after last study drug administration will be recorded in the AE pages of the CRF. A Serious Adverse Event that occurs after this time, including during the follow-up period, if considered related, will be reported.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Ro-CHOP

Reporting group description:

Romidepsin + CHOP 6 cycles

Reporting group title	CHOP

Reporting group description:

CHOP 6 cycles cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP)

Serious adverse events	Ro-CHOP	CHOP	
Total subjects affected by serious adverse events			
subjects affected / exposed	87 / 210 (41.43%)	61 / 208 (29.33%)	
number of deaths (all causes)	110	119	
number of deaths resulting from adverse events	3	4	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasms benign, malignant and unspecified			
subjects affected / exposed	2 / 210 (0.95%)	2 / 208 (0.96%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Vascular disorders			
Vascular disorders			
subjects affected / exposed	5 / 210 (2.38%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	2 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
General disorders			

subjects affected / exposed	16 / 210 (7.62%)	9 / 208 (4.33%)	
occurrences causally related to treatment / all	8 / 20	7 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Immune system disorders			
subjects affected / exposed	0 / 210 (0.00%)	2 / 208 (0.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders			
subjects affected / exposed	8 / 210 (3.81%)	2 / 208 (0.96%)	
occurrences causally related to treatment / all	6 / 8	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Psychiatric disorders			
subjects affected / exposed	1 / 210 (0.48%)	2 / 208 (0.96%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Product issues			
subjects affected / exposed	0 / 210 (0.00%)	1 / 208 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Investigations			
subjects affected / exposed	3 / 210 (1.43%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	4 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications			
subjects affected / exposed	4 / 210 (1.90%)	3 / 208 (1.44%)	
occurrences causally related to treatment / all	1 / 4	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			

Cardiac disorders			
subjects affected / exposed	6 / 210 (2.86%)	6 / 208 (2.88%)	
occurrences causally related to treatment / all	4 / 6	5 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Nervous system disorders			
subjects affected / exposed	4 / 210 (1.90%)	2 / 208 (0.96%)	
occurrences causally related to treatment / all	3 / 4	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Blood and lymphatic system disorders			
subjects affected / exposed	13 / 210 (6.19%)	11 / 208 (5.29%)	
occurrences causally related to treatment / all	13 / 13	7 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastrointestinal disorders			
subjects affected / exposed	11 / 210 (5.24%)	6 / 208 (2.88%)	
occurrences causally related to treatment / all	7 / 12	2 / 6	
deaths causally related to treatment / all	0 / 1	1 / 1	
Hepatobiliary disorders			
Hepatobiliary disorders			
subjects affected / exposed	1 / 210 (0.48%)	2 / 208 (0.96%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Skin and subcutaneous tissue disorders			
Skin and subcutaneous tissue disorders			
subjects affected / exposed	3 / 210 (1.43%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal and urinary disorders			
subjects affected / exposed	2 / 210 (0.95%)	2 / 208 (0.96%)	
occurrences causally related to treatment / all	2 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue			

disorders			
Musculoskeletal and connective tissue disorders			
subjects affected / exposed	3 / 210 (1.43%)	0 / 208 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Infections and Infestations			
subjects affected / exposed	39 / 210 (18.57%)	30 / 208 (14.42%)	
occurrences causally related to treatment / all	26 / 49	18 / 44	
deaths causally related to treatment / all	1 / 1	2 / 2	
Metabolism and nutrition disorders			
Metabolism and nutrition disorders			
subjects affected / exposed	7 / 210 (3.33%)	3 / 208 (1.44%)	
occurrences causally related to treatment / all	9 / 10	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Ro-CHOP	CHOP	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	208 / 210 (99.05%)	203 / 208 (97.60%)	
Vascular disorders			
Vascular disorders			
subjects affected / exposed	29 / 210 (13.81%)	24 / 208 (11.54%)	
occurrences (all)	32	30	
General disorders and administration site conditions			
General disorders and administration site conditions			
subjects affected / exposed	139 / 210 (66.19%)	115 / 208 (55.29%)	
occurrences (all)	278	201	
Respiratory, thoracic and mediastinal disorders			
Respiratory thoracic and mediastinal disorders			
subjects affected / exposed	70 / 210 (33.33%)	48 / 208 (23.08%)	
occurrences (all)	97	60	
Psychiatric disorders			

Psychiatric disorders subjects affected / exposed occurrences (all)	33 / 210 (15.71%) 40	29 / 208 (13.94%) 36	
Investigations Investigations subjects affected / exposed occurrences (all)	133 / 210 (63.33%) 870	92 / 208 (44.23%) 434	
Injury, poisoning and procedural complications Injury, poisoning and procedural complications subjects affected / exposed occurrences (all)	9 / 210 (4.29%) 10	8 / 208 (3.85%) 8	
Cardiac disorders Cardiac disorders subjects affected / exposed occurrences (all)	29 / 210 (13.81%) 35	13 / 208 (6.25%) 16	
Nervous system disorders Nervous system disorders subjects affected / exposed occurrences (all)	93 / 210 (44.29%) 144	80 / 208 (38.46%) 118	
Blood and lymphatic system disorders Blood and lymphatic system disorders subjects affected / exposed occurrences (all)	186 / 210 (88.57%) 1514	126 / 208 (60.58%) 639	
Ear and labyrinth disorders Ear and labyrinth disorders subjects affected / exposed occurrences (all)	11 / 210 (5.24%) 11	7 / 208 (3.37%) 7	
Eye disorders Eye disorders subjects affected / exposed occurrences (all)	11 / 210 (5.24%) 11	10 / 208 (4.81%) 10	
Gastrointestinal disorders Gastrointestinal disorders subjects affected / exposed occurrences (all)	179 / 210 (85.24%) 654	128 / 208 (61.54%) 285	
Hepatobiliary disorders			

Hepatobiliary disorders			
subjects affected / exposed	11 / 210 (5.24%)	5 / 208 (2.40%)	
occurrences (all)	12	8	
Skin and subcutaneous tissue disorders			
Skin and subcutaneous tissue disorders			
subjects affected / exposed	43 / 210 (20.48%)	41 / 208 (19.71%)	
occurrences (all)	59	49	
Renal and urinary disorders			
Renal and urinary disorders			
subjects affected / exposed	13 / 210 (6.19%)	13 / 208 (6.25%)	
occurrences (all)	17	19	
Musculoskeletal and connective tissue disorders			
Musculoskeletal and connective tissue disorders			
subjects affected / exposed	39 / 210 (18.57%)	47 / 208 (22.60%)	
occurrences (all)	57	63	
Infections and infestations			
Infections and infestations			
subjects affected / exposed	104 / 210 (49.52%)	71 / 208 (34.13%)	
occurrences (all)	176	116	
Metabolism and nutrition disorders			
Metabolism and nutrition disorders			
subjects affected / exposed	104 / 210 (49.52%)	33 / 208 (15.87%)	
occurrences (all)	268	101	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 December 2012	- Update of the study rational - Removal of the pretreatment phase within 8 days of randomization - Clarification of the examinations carried out during the treatment phase - Adding of a CT scan between the 3rd and 4th cycle - Modification of the evaluation scheme in the event of progression/relapse - Modification in the frequency of completion of the quality of life questionnaires - Precision of the circuit for inclusion and review of anatomopathological diagnoses - Clarification of sensitivity analyses and overall survival as a primary secondary endpoint - Modification of study management - Modification of principal investigators / Addition of principal investigators - Protocol clarifications and corrections - Adding of the new version investigator brochure

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported