Clinical trial results:
A Phase 2 Randomized Study of Loncastuximab Tesirine Versus Idelalisib in Patients with Relapsed or Refractory Follicular Lymphoma (LOTIS 6)

Summary

EudraCT number	2020-003695-40
Trial protocol	BE PL HU IT ES
Global end of trial date	25 November 2022

Results information

Result version number	v2 (current)
This version publication date	15 October 2023
First version publication date	09 September 2023
Version creation reason	• Correction of full data set Update to free text fields following NIH comments on the ClinicalTrials.Gov results record.

Trial information

Trial identification

Sponsor protocol code	ADCT-402-202

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04699461
WHO universal trial number (UTN)	-
Other trial identifiers	IND Number: 126138

Notes:

Sponsors

Sponsor organisation name	ADC Therapeutics SA
Sponsor organisation address	Route de la Corniche, 3B, Epalinges, Switzerland, 1066
Public contact	Clinical Trials Information, ADC Therapeutics SA, clinicaltrials@adctherapeutics.com
Scientific contact	Clinical Trials Information, ADC Therapeutics SA, clinicaltrials@adctherapeutics.com

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	25 November 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 November 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of single agent loncastuximab tesirine compared to idelalisib in participants with relapsed or refractory follicular lymphoma.

Protection of trial subjects:

The study was performed in accordance with the protocol and with the Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines, applicable International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) Guidelines, and applicable laws and regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 November 2021
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	Hungary: 2
Country: Number of subjects enrolled	Poland: 2
Country: Number of subjects enrolled	Spain: 2
Worldwide total number of subjects	6
EEA total number of subjects	6

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)	5

From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at research centers in Spain, Hungary and Poland from November 2021 to November 2022. Only 6 participants were enrolled and the study was terminated early (administrative decision).

Pre-assignment

Screening details:

Eligible participants were randomly assigned in a 2:1 ratio to treatment with loncastuximab tesirine or idelalisib.

Period 1

Period 1 title	Overall Period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Loncastuximab Tesirine

Arm description:

Participants were administered loncastuximab tesirine as an intravenous (IV) infusion on Day 1 of each cycle, where 1 cycle is 3 weeks. Loncastuximab tesirine was administered at a dose of 150 µg/kg for 2 cycles, then at a dose of 75 µg/kg for subsequent cycles. The median number of treatment cycles was 5.5 (min: 5; max: 12). The median treatment duration was 122.5 days (min: 54; max: 231 days).

Arm type	Experimental
Investigational medicinal product name	Loncastuximab Tesirine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

IV infusion on Day 1 of each cycle. Loncastuximab tesirine was administered at 150 µg/kg for 2 cycles, then at a dose of 75 µg/kg for subsequent cycles.

Arm title	Idelalisib

Arm description:

Participants were administered 150 mg idelalisib, orally, twice a day throughout each cycle, where 1 cycle is 4 weeks. 1 participant received 6 cycles and the other participant received 13 cycles of treatment. The treatment duration was 140 days and 333 days, respectively.

Arm type	Active comparator
Investigational medicinal product name	Idelalisib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

150 mg orally, twice a day on Day 1 of each cycle.

Number of subjects in period 1	Loncastuximab Tesirine	Idelalisib
Started	4	2
Completed	0	0
Not completed	4	2
Adverse event, serious fatal	1	-
Consent withdrawn by subject	1	-
Radiographic progression	-	1
Study termination by sponsor	2	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall Period

Reporting group description: -

Reporting group values	Overall Period	Total	
Number of subjects	6	6	
Age categorical Units: Subjects			
Age 55 to 69 years	6	6	
Age continuous Units: years median full range (min-max)	 57 55 to 69	 -	
Gender categorical Units: Subjects			
Female	4	4	
Male	2	2	

End points

End points reporting groups

Reporting group title	Loncastuximab Tesirine

Reporting group description:

Participants were administered loncastuximab tesirine as an intravenous (IV) infusion on Day 1 of each cycle, where 1 cycle is 3 weeks. Loncastuximab tesirine was administered at a dose of 150 µg/kg for 2 cycles, then at a dose of 75 µg/kg for subsequent cycles. The median number of treatment cycles was 5.5 (min: 5; max: 12). The median treatment duration was 122.5 days (min: 54; max: 231 days).

Reporting group title	Idelalisib

Reporting group description:

Participants were administered 150 mg idelalisib, orally, twice a day throughout each cycle, where 1 cycle is 4 weeks. 1 participant received 6 cycles and the other participant received 13 cycles of treatment. The treatment duration was 140 days and 333 days, respectively.

Primary: Complete Response Rate (CRR)

End point title	Complete Response Rate (CRR)[1]

End point description:

CRR was defined as the percentage of participants who experienced a best overall response (BOR) of complete response (CR) assessed prior to any subsequent anticancer treatment.

End point type	Primary

End point timeframe:

Up to the end of treatment, maximum time on treatment was 333 days

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: No additional statistical analyses were pre-specified for this endpoint.

End point values	Loncastuximab Tesirine	Idelalisib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: Percentage of participants				
number (not applicable)				

Notes:

[2] - No response data was collected.

[3] - No response data was collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate (ORR)

End point title	Overall Response Rate (ORR)

End point description:

ORR was defined as the percentage of participants with a BOR of CR or partial response (PR) assessed prior to any subsequent anticancer treatment.

End point type	Secondary

End point timeframe:

Up to end of treatment, maximum time on treatment was 333 days

End point values	Loncastuximab Tesirine	Idelalisib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[4]	0[5]		
Units: Percentage of participants				
number (not applicable)				

Notes:

[4] - No response data was collected.

[5] - No response data was collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS)

End point title	Progression-Free Survival (PFS)

End point description:

PFS was defined as the time between the randomization date and the first documentation of recurrence, progression, or death.

Values of "99999" indicate N/A due to risk of reidentification.

End point type	Secondary

End point timeframe:

Up to end of treatment, maximum time on treatment was 333 days

End point values	Loncastuximab Tesirine	Idelalisib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1[6]	1[7]		
Units: Days				
median (full range (min-max))	99999 (99999 to 99999)	99999 (99999 to 99999)		

Notes:

[6] - Inclusive of participants who experienced recurrence, progression, or death.

[7] - Inclusive of participants who experienced recurrence, progression, or death.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS was defined as the time between the randomization date and death from any cause.

Values of "99999" indicate N/A due to risk of reidentification.

End point type	Secondary

End point timeframe:

Up to end of treatment, maximum time on treatment was 333 days

End point values	Loncastuximab Tesirine	Idelalisib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1[8]	0[9]		
Units: Days				
median (full range (min-max))	99999 (99999 to 99999)	(to)		

Notes:

[8] - Inclusive of participants who experienced death.

[9] - Inclusive of participants who experienced death.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)

End point description:

DOR was defined as the time from the documentation of tumor response to disease progression or death.

End point type	Secondary

End point timeframe:

Up to end of treatment, maximum time on treatment was 333 days

End point values	Loncastuximab Tesirine	Idelalisib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[10]	0[11]		
Units: Days				
median (confidence interval 95%)	(to)	(to)		

Notes:

[10] - No response data was collected.

[11] - No response data was collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Experience at Least One Treatment-Emergent Adverse Event (TEAE)

End point title	Number of Participants Who Experience at Least One Treatment-Emergent Adverse Event (TEAE)

End point description:

TEAEs were defined as an AE that occurs or worsens in the period extending from the first dose of study treatment until 30 days after the last dose of study treatment or start of new anti-cancer therapy, whichever is earlier.

Any clinically significant changes from baseline in the safety laboratory values, vital signs, 12-lead electrocardiogram (ECG), and Eastern Cooperative Oncology Group (ECOG) performance status were reported as TEAEs.

End point type	Secondary

End point timeframe:

Day 1 to 30 days after end of treatment, maximum time on treatment was 333 days

End point values	Loncastuximab Tesirine	Idelalisib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	2		
Units: Participants				
TEAEs	4	2		
Serious TEAEs	3	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Average Concentration of Loncastuximab Tesirine Before Infusion

End point title	Average Concentration of Loncastuximab Tesirine Before Infusion

End point description:

End point type	Secondary

End point timeframe:

Up to end of treatment, maximum time on treatment was 333 days

End point values	Loncastuximab Tesirine	Idelalisib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[12]	0[13]		
Units: ng/mL				
arithmetic mean (standard deviation)	()	()		

Notes:

[12] - No data was collected.

[13] - No data was collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Average Concentration of Loncastuximab Tesirine at the End of Infusion

End point title	Average Concentration of Loncastuximab Tesirine at the End of Infusion

End point description:

End point type	Secondary

End point timeframe:

Up to end of treatment, maximum time on treatment was 333 days

End point values	Loncastuximab Tesirine	Idelalisib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[14]	0[15]		
Units: ng/mL				
arithmetic mean (standard deviation)	()	()		

Notes:

[14] - No data was collected.

[15] - No data was collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Clearance Rate of Loncastuximab Tesirine

End point title	Clearance Rate of Loncastuximab Tesirine

End point description:

End point type	Secondary

End point timeframe:

Up to end of treatment, maximum time on treatment was 333 days

End point values	Loncastuximab Tesirine	Idelalisib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[16]	0[17]		
Units: Litres/hour				
arithmetic mean (standard deviation)	()	()		

Notes:

[16] - No data was collected.

[17] - No data was collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Volume of Distribution of Loncastuximab Tesirine

End point title	Volume of Distribution of Loncastuximab Tesirine

End point description:

End point type	Secondary

End point timeframe:

Up to end of treatment, maximum time on treatment was 333 days

End point values	Loncastuximab Tesirine	Idelalisib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[18]	0[19]		
Units: Litres				
arithmetic mean (standard deviation)	()	()		

Notes:

[18] - No data was collected.

[19] - No data was collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Anti-Drug Antibody (ADA) Titers to Loncastuximab Tesirine

End point title	Number of Participants With Anti-Drug Antibody (ADA) Titers to Loncastuximab Tesirine

End point description:

End point type	Secondary

End point timeframe:

Up to end of treatment, maximum time on treatment was 333 days

End point values	Loncastuximab Tesirine	Idelalisib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[20]	0[21]		
Units: Participants				

Notes:

[20] - No data was collected.

[21] - No data was collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Health-Related Quality of Life (HRQoL) as Measured by the EuroQol-5 Dimensions-5 Levels (EQ-5D-5L)

End point title	Change From Baseline in Health-Related Quality of Life (HRQoL) as Measured by the EuroQol-5 Dimensions-5 Levels (EQ-5D-5L)

End point description:

End point type	Secondary

End point timeframe:

Up to end of treatment, maximum time on treatment was 333 days

End point values	Loncastuximab Tesirine	Idelalisib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[22]	0[23]		
Units: Score on a scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[22] - No data was collected.

[23] - No data was collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Health-Related Quality of Life (HRQoL) as Measured by the Functional Assessment of Cancer Therapy-Lymphoma (FACT-Lym)

End point title	Change From Baseline in Health-Related Quality of Life (HRQoL) as Measured by the Functional Assessment of Cancer Therapy-Lymphoma (FACT-Lym)

End point description:

End point type	Secondary

End point timeframe:

Up to end of treatment, maximum time on treatment was 333 days

End point values	Loncastuximab Tesirine	Idelalisib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[24]	0[25]		
Units: Score on a scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[24] - No data was collected.

[25] - No data was collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Specific Symptomatic Adverse Event Symptoms As Selected From Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE)

End point title	Number of Participants With Specific Symptomatic Adverse Event Symptoms As Selected From Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE)

End point description:

The specific symptomatic adverse events includes fatigue, swelling, rash, nausea, diarrhea, abdominal pain, and cough.

End point type	Secondary

End point timeframe:

Up to end of treatment, maximum time on treatment was 333 days

End point values	Loncastuximab Tesirine	Idelalisib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[26]	0[27]		
Units: Participants				

Notes:

[26] - No data was collected.

[27] - No data was collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment-Related Symptoms as Assessed by Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE)

End point title	Treatment-Related Symptoms as Assessed by Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE)

End point description:

The specific symptoms assessed include fatigue, swelling, rash, nausea, diarrhea, abdominal pain, and cough. The severity is assessed from "None" to "Very severe" and the interference level is assessed from "Not at all" to "Very much."

End point type	Secondary

End point timeframe:

Up to end of treatment, maximum time on treatment was 333 days

End point values	Loncastuximab Tesirine	Idelalisib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[28]	0[29]		
Units: Participants				

Notes:

[28] - No data was collected.

[29] - No data was collected.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to end of treatment, maximum time on treatment was 333 days

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Idelalisib

Reporting group description:

Participants were administered 150 mg idelalisib, orally, twice a day throughout each cycle, where 1 cycle is 4 weeks. 1 participant received 6 cycles and the other participant received 13 cycles of treatment. The treatment duration was 140 days and 333 days, respectively.

Reporting group title	Loncastuximab Tesirine

Reporting group description:

Participants were administered loncastuximab tesirine as an intravenous (IV) infusion on Day 1 of each cycle, where 1 cycle is 3 weeks. Loncastuximab tesirine was administered at a dose of 150 µg/kg for 2 cycles, then at a dose of 75 µg/kg for subsequent cycles. The median number of treatment cycles was 5.5 (min: 5; max: 12). The median treatment duration was 122.5 days (min: 54; max: 231 days).

Serious adverse events	Idelalisib	Loncastuximab Tesirine	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	3 / 4 (75.00%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 2 (0.00%)	2 / 4 (50.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	0 / 2 (0.00%)	2 / 4 (50.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Idelalisib	Loncastuximab Tesirine	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)	4 / 4 (100.00%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 2 (100.00%)	1 / 4 (25.00%)	
occurrences (all)	6	1	
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 2 (100.00%)	1 / 4 (25.00%)	
occurrences (all)	5	2	
Blood creatinine increased			
subjects affected / exposed	1 / 2 (50.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Lipase increased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	2	
Neutropenia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	2	
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Dysphagia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Malaise			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Odynophagia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Abdominal pain			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Porphyria non-acute			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Dyspnea			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Cough			
subjects affected / exposed	1 / 2 (50.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Seborrheic keratosis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	

Infections and infestations COVID-19 infection subjects affected / exposed occurrences (all) Oral candidiasis subjects affected / exposed occurrences (all) COVID-19 pneumonia subjects affected / exposed occurrences (all)	 1 / 2 (50.00%) 1 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0	 2 / 4 (50.00%) 2 1 / 4 (25.00%) 1 2 / 4 (50.00%) 2	
Metabolism and nutrition disorders Hyperglycemia subjects affected / exposed occurrences (all)	 0 / 2 (0.00%) 0	 1 / 4 (25.00%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 November 2020	The primary reason for Protocol Amendment 1 was to incorporate the changes in response to the US FDA feedback. This amendment combines changes regarding safety monitoring, study stratification, and statistical analysis. In addition, updates include removal of QTcF eligibility criteria and dexamethasone equivalent as premedication, assigning ORR as key secondary endpoint, as well as modifications on PRO schedules.
19 February 2021	The primary reason for Protocol Amendment 2 was to extend the contraception duration post loncastuximab tesirine for female participants with childbearing potential from 6 to 9 months to align with current regulatory guidance.
07 April 2021	The primary reason for Protocol Amendment 3 is to align the frequency of laboratory evaluations for participants treated with idelalisib with the idelalisib Summary of Product Characteristics (SmPC); to exclude participants with history of hypersensitivity to any of the excipients of study drugs; to align contraception guidance for women of childbearing potential (WOCBP) receiving idelalisib treatment with the idelalisib SmPC; and to extend SAE reporting duration to at least 5 half-lives after the last loncastuximab tesirine dose based on regulatory authority request.

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.

The study was terminated due to administrative decision (not due to safety reason) by the sponsor following the withdrawal of idelalisib from the US market for the relapsed FL indication (i.e., not due to any safety reasons emerging from this study).

Notes: