Clinical trial results:
An Open-label Extension to the Phase 2 Randomized, Double-blind, Placebo-controlled, Crossover Multicenter Study to Evaluate the Safety and Efficacy of KZR-616 in the Treatment of Patients with Active Polymyositis or Dermatomyositis

Summary

EudraCT number	2020-004382-39
Trial protocol	CZ
Global end of trial date	12 June 2023

Results information

Result version number	v1 (current)
This version publication date	27 June 2024
First version publication date	27 June 2024

Trial information

Trial identification

Sponsor protocol code	KZR-616-003E

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04628936
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Kezar Life Sciences, Inc.
Sponsor organisation address	4000 Shoreline Court, Suite 300, South San Francisco, United States, 94080
Public contact	Regulatory Affairs, Kezar Life Sciences, Inc., 001 6508225600, PRESIDIO@kezarbio.com
Scientific contact	Clinical Science, Kezar Life Sciences, Inc., 001 6508225600, PRESIDIO@kezarbio.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	27 July 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 March 2023
Global end of trial reached?	Yes
Global end of trial date	12 June 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Efficacy: To evaluate the long-term efficacy of zetomipzomib (KZR-616) in patients with PM or DM.
Safety: To evaluate the long-term safety and tolerability of zetomipzomib (KZR-616) in patients with PM or DM.

Protection of trial subjects:

Investigators and all parties involved in this study conducted the study in adherence to the ethical principles based on the Declaration of Helsinki, ICH guidelines for cGCP, and the applicable laws and regulatory requirements.
IRB/IEC approval of the study and relevant study information (e.g. protocol, informed consent form (ICF), patient-facing materials) was obtained before initiation of study sites or releasing study drug to sites. Extensions/renewals of the approval were obtained as necessary.
Written informed consent (signed and dated) was obtained before any study-related procedures were performed. Patients were given every opportunity to ask for clarification and were given ample time to consider the study. Patients may refuse to enter the study or to withdraw from the study at any time, without consequences for their further care or penalty or loss of benefits to which the patient is otherwise entitled.
All Investigators promptly reported any new information that may have adversely affected patient safety or the study conduct and submitted study status summaries to the IRB/IEC as required. Patients were informed about new information available that was relevant to their willingness to continue participation in the study and were reconsented to the IRB/IEC/regulatory authorities currently approved ICF.
Patients' identity remained confidential in any presentations or publications of the study results. All personal data collected and processed for the purposes of this study were managed with adequate precautions to ensure confidentiality of data, and in accordance with the applicable laws and regulations on personal data protection.
A study-specific Data Monitoring Committee met to review accumulating safety data, study conduct and progress and to make recommendations about the study progress on a regular basis. Each voting member provided their recommendation at the conclusion of each meeting.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 November 2020
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	United States: 17
Country: Number of subjects enrolled	Czechia: 1
Worldwide total number of subjects	18
EEA total number of subjects	1

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	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This was an optional open-label extension to Study KZR-616-003 (EudraCT Number: 2019-002605-22). Twenty patients completed the KZR-616-003 study and were eligible to enroll in the open-label extension.

Pre-assignment period milestones

Number of subjects started	18
Number of subjects completed	18

Period 1

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

Arms

Arm title	KZR-616 45 mg + Standard Therapy (Open-label)

Arm description:

All patients received SC injections of KZR-616 QW at doses of 30 mg on day 1 and 45 mg thereafter for up to 96 weeks. Study drug administration ended when the last enrolled patient completed 48 weeks of dosing in the OLE. Patients had an end of study visit 12 weeks after the last dose of KZR-616.

KZR-616: zetomipzomib subcutaneous injection

Arm type	Experimental
Investigational medicinal product name	zetomipzomib
Investigational medicinal product code	
Other name	KZR-616
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

All patients received a SC injection of 30 mg KZR-616 at Visit 1 (Day 1), followed by weekly SC injections of 45 mg KZR-616 up to a maximum of 96 weeks. Study drug administration ended for all patients in Study KZR-616-003E when the last patient enrolled completed 48 weeks of dosing.

Number of subjects in period 1	KZR-616 45 mg + Standard Therapy (Open-label)
Started	18
Completed	8
Not completed	10
Consent withdrawn by subject	9
Adverse event, non-fatal	1

Baseline characteristics

Reporting groups	
Reporting group title	Open Label Extension

Reporting group description: -

Reporting group values	Open Label Extension	Total	
Number of subjects	18	18	
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)	15	15	
From 65-84 years	3	3	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	52.7		
standard deviation	± 14.3	-	
Gender categorical Units: Subjects			
Female	13	13	
Male	5	5	

End points

End points reporting groups

Reporting group title	KZR-616 45 mg + Standard Therapy (Open-label)

Reporting group description:

All patients received SC injections of KZR-616 QW at doses of 30 mg on day 1 and 45 mg thereafter for up to 96 weeks. Study drug administration ended when the last enrolled patient completed 48 weeks of dosing in the OLE. Patients had an end of study visit 12 weeks after the last dose of KZR-616.

KZR-616: zetomipzomib subcutaneous injection

Subject analysis set title	KZR-616 45 mg + Standard Therapy (Open-label)
Subject analysis set type	Full analysis

Subject analysis set description:

All patients received SC injections of KZR-616 QW at doses of 30 mg on day 1 and 45 mg thereafter for up to 96 weeks. Study drug administration ended when the last enrolled patient completed 48 weeks of dosing in the OLE. Patients had an end of study visit 12 weeks after the last dose of KZR-616.

KZR-616: zetomipzomib subcutaneous injection

Primary: Mean Total Improvement Score (TIS) at OLE Week 48

End point title	Mean Total Improvement Score (TIS) at OLE Week 48[1]

End point description:

The mean Total Improvement Score (TIS) at OLE Week 48, which ranges from 0 to 100 [low of 0 to high of 100, where higher scores are better]. The timeframe of 48 weeks was selected because it represented the maximum timeframe of dosing for the last patient enrolled as the study drug administration ended when the last patient enrolled completed 48 weeks of dosing.

End point type	Primary

End point timeframe:

48 weeks

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: Study KZR-616-003E was an open-label extension study which was descriptive in nature, and no formal hypothesis testing was performed. No formal statistical sample size estimation was performed, since the number of patients in this study was determined by the number of patients who completed Study KZR-616-003 and enrolled in the OLE study.

End point values	KZR-616 45 mg + Standard Therapy (Open-label)			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: score on a scale				
arithmetic mean (standard deviation)	36.4 (± 23.2)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 108 weeks

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	KZR-616 45 mg + Standard Therapy (Open-label)

Reporting group description:

All patients received SC injections of KZR-616 QW at doses of 30 mg on day 1 and 45 mg thereafter for up to 96 weeks. Study drug administration ended when the last enrolled patient completed 48 weeks of dosing in the OLE. Patients had an end of study visit 12 weeks after the last dose of KZR-616.

KZR-616: zetomipzomib subcutaneous injection

Serious adverse events	KZR-616 45 mg + Standard Therapy (Open-label)		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 18 (5.56%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Wellens' syndrome			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	KZR-616 45 mg + Standard Therapy (Open-label)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 18 (94.44%)		
Vascular disorders			
Hot flush			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	2		
Hypertension			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	3		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Chest pain			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Chills			
subjects affected / exposed	4 / 18 (22.22%)		
occurrences (all)	14		
Fatigue			
subjects affected / exposed	3 / 18 (16.67%)		
occurrences (all)	41		
Influenza like illness			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Infusion site reaction			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Injection site bruising			
subjects affected / exposed	3 / 18 (16.67%)		
occurrences (all)	47		
Injection site erythema			
subjects affected / exposed	4 / 18 (22.22%)		
occurrences (all)	98		
Injection site exfoliation			

subjects affected / exposed	1 / 18 (5.56%)			
occurrences (all)	2			
Injection site induration				
subjects affected / exposed	3 / 18 (16.67%)			
occurrences (all)	6			
Injection site inflammation				
subjects affected / exposed	1 / 18 (5.56%)			
occurrences (all)	1			
Injection site irritation				
subjects affected / exposed	1 / 18 (5.56%)			
occurrences (all)	2			
Injection site pain				
subjects affected / exposed	1 / 18 (5.56%)			
occurrences (all)	10			
Injection site pruritus				
subjects affected / exposed	2 / 18 (11.11%)			
occurrences (all)	24			
Injection site rash				
subjects affected / exposed	1 / 18 (5.56%)			
occurrences (all)	1			
Injection site reaction				
subjects affected / exposed	8 / 18 (44.44%)			
occurrences (all)	177			
Injection site swelling				
subjects affected / exposed	2 / 18 (11.11%)			
occurrences (all)	33			
Injection site urticaria				
subjects affected / exposed	1 / 18 (5.56%)			
occurrences (all)	1			
Injection site vesicles				
subjects affected / exposed	1 / 18 (5.56%)			
occurrences (all)	1			
Oedema peripheral				
subjects affected / exposed	1 / 18 (5.56%)			
occurrences (all)	1			
Pain				

subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all) Vaccination site pain subjects affected / exposed occurrences (all)	5 / 18 (27.78%) 38 5 / 18 (27.78%) 18 1 / 18 (5.56%) 1		
Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all)	 1 / 18 (5.56%) 3		
Reproductive system and breast disorders Menopausal symptoms subjects affected / exposed occurrences (all)	 1 / 18 (5.56%) 1		
Respiratory, thoracic and mediastinal disorders Epistaxis subjects affected / exposed occurrences (all) Nasal congestion subjects affected / exposed occurrences (all)	 1 / 18 (5.56%) 2 1 / 18 (5.56%) 1		
Investigations Reticulocyte count increased subjects affected / exposed occurrences (all) White blood cell count decreased subjects affected / exposed occurrences (all)	 1 / 18 (5.56%) 1 1 / 18 (5.56%) 1		
Injury, poisoning and procedural complications Administration related reaction subjects affected / exposed occurrences (all) Contusion	 1 / 18 (5.56%) 2		

subjects affected / exposed	3 / 18 (16.67%)		
occurrences (all)	4		
Fall			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Injection related reaction			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Ligament sprain			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	2		
Post vaccination syndrome			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	4		
Underdose			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Diastolic dysfunction			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Pericardial effusion			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Headache			
subjects affected / exposed	5 / 18 (27.78%)		
occurrences (all)	9		
Migraine			

subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Eye disorders			
Dry eye			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Keratitis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	2		
Abdominal pain upper			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	5 / 18 (27.78%)		
occurrences (all)	6		
Diverticulum intestinal			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Dysphagia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Hiatus hernia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Nausea			

subjects affected / exposed	6 / 18 (33.33%)		
occurrences (all)	31		
Vomiting			
subjects affected / exposed	4 / 18 (22.22%)		
occurrences (all)	8		
Hepatobiliary disorders			
Biliary dilatation			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Cholelithiasis			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Hyperbilirubinaemia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Jaundice			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Dermatomyositis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	4		
Pruritus			
subjects affected / exposed	3 / 18 (16.67%)		
occurrences (all)	10		
Rash papular			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	2		
Skin hyperpigmentation			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Urticaria			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Renal and urinary disorders			

Dysuria			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Hydronephrosis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	2		
Ureterolithiasis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 18 (16.67%)		
occurrences (all)	4		
Costochondritis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Joint swelling			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Muscular weakness			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Infections and infestations			
Adenovirus infection			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
COVID-19			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Gastroenteritis viral			

subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	3		
Upper respiratory tract infection			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	3		
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Vulvovaginal mycotic infection			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Urinary tract infection			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Urinary tract infection bacterial			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Abnormal weight gain			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Hyperkalaemia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Hypoglycaemia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 September 2021	Protocol amended to extend weekly KZR-616 administration until the last patient enrolled completed 48 weeks of dosing, and to support optional at-home KZR-616 administration by patients and caregivers.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported