



Clinical trial results:

A 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	2019-002605-22
Trial protocol	CZ DE
Global end of trial date	06 April 2022

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-616-003
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04033926
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	06 April 2022
Global end of trial reached?	Yes
Global end of trial date	06 April 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate efficacy of KZR-616 in patient with Polymyositis (PM) or Dermatomyositis (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 (Safety Review Committee per BfArM) 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	14 January 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	Czechia: 1
Country: Number of subjects enrolled	United States: 24
Worldwide total number of subjects	25
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)	21
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Study entry criteria included adults with PM or DM based on the 2017 EULAR/ACR Classification Criteria with confirmed active disease (MMT-8 score of 80-136 [0-150] and two other abnormal core set measures) and inadequate response to 12 weeks of corticosteroids or at least one (1) immunosuppressant.

Period 1

Period 1 title	Treatment Period 1
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	No
Arm title	Arm A: Period 1 (Zetomipzomib)

Arm description:

Zetomipzomib 30 mg SC weekly for 2 weeks, then 45 mg SC weekly for 14 weeks

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:

30 mg subcutaneous injections of zetomipzomib once weekly for the first two weeks, then 45 mg zetomipzomib SC QW for the remaining 14 weeks of treatment

Arm title	Arm B: Period 1 (Placebo)
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Arm description:

Placebo SC weekly for 16 weeks

Arm type	Placebo
Investigational medicinal product name	sterile water for injection
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solvent for parenteral use
Routes of administration	Subcutaneous use

Dosage and administration details:

Matching placebo was administered by SC injection QW to patients in Arm B during Period 1 and patients in Arm A during Period 2.

Number of subjects in period 1	Arm A: Period 1 (Zetomipzomib)	Arm B: Period 1 (Placebo)
Started	13	12
Completed	10	12
Not completed	3	0
Consent withdrawn by subject	3	-

Period 2

Period 2 title	Treatment Period 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	No
Arm title	Arm A: Period 2 (Placebo)

Arm description:

Placebo SC weekly for 16 weeks

Arm type	Placebo
Investigational medicinal product name	sterile water for injection
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solvent for parenteral use
Routes of administration	Subcutaneous use

Dosage and administration details:

Matching placebo was administered by SC injection QW to patients in Arm B during Period 1 and patients in Arm A during Period 2.

Arm title	Arm B: Period 2 (Zetomipzomib)
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Arm description:

Zetomipzomib 30 mg SC weekly for 2 weeks, then 45 mg SC weekly for 14 weeks

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:

30 mg subcutaneous injections of zetomipzomib once weekly for the first two weeks, then 45 mg zetomipzomib SC QW for the remaining 14 weeks of treatment

Number of subjects in period 2	Arm A: Period 2 (Placebo)	Arm B: Period 2 (Zetomipzomib)
Started	10	12
Completed	8	12
Not completed	2	0
Consent withdrawn by subject	1	-
Investigator decision	1	-

Baseline characteristics

Reporting groups

Reporting group title	Treatment Period 1
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Reporting group description: -

Reporting group values	Treatment Period 1	Total	
Number of subjects	25	25	
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)	21	21	
From 65-84 years	4	4	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	51.6		
standard deviation	± 13.7	-	
Gender categorical			
Units: Subjects			
Female	18	18	
Male	7	7	

End points

End points reporting groups

Reporting group title	Arm A: Period 1 (Zetomipzomib)
Reporting group description: Zetomipzomib 30 mg SC weekly for 2 weeks, then 45 mg SC weekly for 14 weeks	
Reporting group title	Arm B: Period 1 (Placebo)
Reporting group description: Placebo SC weekly for 16 weeks	
Reporting group title	Arm A: Period 2 (Placebo)
Reporting group description: Placebo SC weekly for 16 weeks	
Reporting group title	Arm B: Period 2 (Zetomipzomib)
Reporting group description: Zetomipzomib 30 mg SC weekly for 2 weeks, then 45 mg SC weekly for 14 weeks	
Subject analysis set title	Arm A: Period 1 (Zetomipzomib)
Subject analysis set type	Full analysis
Subject analysis set description: Zetomipzomib 30 mg SC weekly for 2 weeks, then 45 mg SC weekly for 14 weeks	
Subject analysis set title	Arm B: Period 1 (Placebo)
Subject analysis set type	Full analysis
Subject analysis set description: Placebo SC weekly for 16 weeks	
Subject analysis set title	Arm A: Period 2 (Placebo)
Subject analysis set type	Full analysis
Subject analysis set description: Placebo SC weekly for 16 weeks	
Subject analysis set title	Arm B: Period 2 (Zetomipzomib)
Subject analysis set type	Full analysis
Subject analysis set description: Zetomipzomib 30 mg SC weekly for 2 weeks, then 45 mg SC weekly for 14 weeks	
Subject analysis set title	Zetomipzomib First, Then Placebo (Arm A)
Subject analysis set type	Full analysis
Subject analysis set description: Treatment Period 1: Zetomipzomib 30 mg SC weekly for 2 weeks, then 45 mg SC weekly for 14 weeks Treatment Period 2: Placebo SC weekly for 16 weeks	
Subject analysis set title	Placebo First, Then Zetomipzomib (Arm B)
Subject analysis set type	Full analysis
Subject analysis set description: Treatment Period 1: Placebo SC weekly for 16 weeks Treatment Period 2: Zetomipzomib 30 mg SC weekly for 2 weeks, then 45 mg SC weekly for 14 weeks	
Subject analysis set title	Arm A: Period 1 + Arm B: Period 2
Subject analysis set type	Full analysis
Subject analysis set description: All patients treated with zetomipzomib.	
Arm A - Treatment Period 1: Zetomipzomib 30 mg SC weekly for 2 weeks, then 45 mg SC weekly for 14 weeks	
Arm B - Treatment Period 2: Zetomipzomib 30 mg SC weekly for 2 weeks, then 45 mg SC weekly for 14 weeks	
Subject analysis set title	Baseline
Subject analysis set type	Full analysis

Subject analysis set description:

For the statistical analysis of the primary endpoint, Total Improvement Score (TIS) was assessed using Week 0 as the baseline (before zetomipzomib [KZR-616] administration) timepoint for both Arm A and Arm B patients.

Primary: Mean Change in the Total Improvement Score (TIS) From Start to End of Zetomipzomib (KZR-616) Treatment Period

End point title	Mean Change in the Total Improvement Score (TIS) From Start to End of Zetomipzomib (KZR-616) Treatment Period
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End point description:

The primary efficacy endpoint was mean change from start to end of zetomipzomib (KZR-616) Treatment Periods in the Total Improvement Score (TIS), which ranges from 0 to 100 [low of 0 to high of 100, where higher scores are better]. Mean change in TIS was calculated by comparing the Baseline and post Baseline observations for patients in both KZR-616 treatment periods combined.

Note: TIS scores for placebo treatment periods are presented in this outcome measure but were not included in the primary outcome measure analysis.

End point type	Primary
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End point timeframe:

16 weeks in each Treatment Period (32 weeks total)

End point values	Arm A: Period 1 (Zetomipzomib)	Arm B: Period 1 (Placebo)	Arm A: Period 2 (Placebo)	Arm B: Period 2 (Zetomipzomib)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	12	8	12
Units: score on a scale				
arithmetic mean (standard deviation)	25.5 (± 18.6)	25.0 (± 19.9)	33.1 (± 17.6)	33.5 (± 22.9)

End point values	Arm A: Period 1 + Arm B: Period 2	Baseline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	22	22		
Units: score on a scale				
arithmetic mean (standard deviation)	28.8 (± 3.7)	0 (± 0)		

Statistical analyses

Statistical analysis title	Change in Score from Baseline
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Statistical analysis description:

Mean change in TIS was calculated by comparing the baseline and post baseline observations within patients for the zetomipzomib (KZR-616) treatment periods combined (Arm A: Period 1 + Arm B: Period 2).

Due to system limitations, the number of "Subjects in this analysis" reads 44 but should be 22. This discrepancy occurs from subjects being counted twice, once at baseline group and once in the treatment group, even though they should only be counted once.

Comparison groups	Arm A: Period 1 + Arm B: Period 2 v Baseline
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other ^[1]
P-value	= 0.0001
Method	mixed model repeated measures

Notes:

[1] - The mixed model repeated measures (MMRM) statistical approach was used for this analysis. The MMRM statistical approach was used for this analysis since it is preferred in Longitudinal Clinical Trial Data with missing data and increases the power by allowing for more data to be incorporated from different timepoints.

Secondary: Proportion of Patients With TIS Response

End point title	Proportion of Patients With TIS Response
End point description:	
The proportion of patients with an increase of ≥ 20 points on the TIS from start to end of zetomipzomib (KZR-616) treatment. TIS response is categorized by the following improvement thresholds: Minimal response = TIS ≥ 20 Moderate response = TIS ≥ 40 Major response = TIS ≥ 60 This endpoint was assessed by comparing Week 16 versus Week 0 for patients allocated to Arm A and Week 32 versus Week 16 for patients allocated to Arm B. This re-baselining approach was utilized to maximize the precision for assessment of zetomipzomib effect in Arm B.	
End point type	Secondary
End point timeframe:	
32 weeks	

End point values	Arm A: Period 1 (Zetomipzomib)	Arm B: Period 1 (Placebo)	Arm A: Period 2 (Placebo)	Arm B: Period 2 (Zetomipzomib)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	12	8	12
Units: participants				
Minimal response	6	7	1	6
Moderate response	2	2	1	2
Major response	0	1	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Patients Meeting the International Myositis Assessment and Clinical Studies Group (IMACS) Definition of Improvement (DOI)

End point title	Proportion of Patients Meeting the International Myositis Assessment and Clinical Studies Group (IMACS) Definition of Improvement (DOI)
End point description:	
The IMACS DOI is $\geq 20\%$ improvement in at least 3 of 6 core set activity measures, with no more than 2 core set activity measures (CSAMs) worsening by $\geq 25\%$ (Manual Muscle Testing-8 Muscle Groups [MMT-8] could not be a worsening measure).	

End point type	Secondary
End point timeframe:	
32 weeks	

End point values	Arm A: Period 1 (Zetomipzomib)	Arm B: Period 1 (Placebo)	Arm A: Period 2 (Placebo)	Arm B: Period 2 (Zetomipzomib)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	13	12	10	12
Units: proportion of participants				
number (confidence interval 95%)	7.7 (0.25 to 44.50)	8.3 (0.21 to 38.48)	10.0 (0.32 to 52.65)	25.0 (5.49 to 57.19)

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Percent Change From Baseline From Start to End of Treatment in the IMACS Individual CSAMs

End point title	Mean Percent Change From Baseline From Start to End of Treatment in the IMACS Individual CSAMs
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End point description:

Mean percent change from baseline of the IMACS CSAMs which consists of:

Physician Global Assessment (MDGA) - 5 point Likert scale and 10cm Visual Analogue Scale

Patient Global Assessments of Disease Activity (PtGADA) - 10cm Visual Analogue Scale

Manual Muscle Testing-8 Muscle Groups (MMT-8) - scores range from 0 - 260, high scores are better

Health Assessment Questionnaire-Disability Index (HAQ-DI) - scores range from 0 - 3, high scores are worse

Myositis Disease Activity Assessment Tool (MDAAT, 2005 version) - scores range from 0 - 60, high scores are worse

Muscle enzymes (clinical laboratory assessments): Summarize the most abnormal clinical laboratory assessment at baseline between creatine kinase (CK), aldolase, lactate dehydrogenase (LDH), alanine aminotransferase (ALT), and aspartate aminotransferase (AST).

End point type	Secondary
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End point timeframe:

32 weeks

End point values	Arm A: Period 1 (Zetomipzomib)	Arm B: Period 1 (Placebo)	Arm A: Period 2 (Placebo)	Arm B: Period 2 (Zetomipzomib)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	12	8	12
Units: score on a scale				
arithmetic mean (standard deviation)				
MDGA	-32.5 (± 35.1)	-22.1 (± 36.8)	81.7 (± 204.3)	-4.5 (± 58.6)
PtGADA	-23.1 (± 35.1)	-21.7 (± 49.8)	48.6 (± 121.4)	64.4 (± 163.8)
MMT-8	6.7 (± 8.6)	5.6 (± 6.1)	0.2 (± 4.6)	1.5 (± 7.1)

HAQ-DI	-28.2 (± 34.4)	1.2 (± 80.5)	19.2 (± 51.2)	-8.8 (± 60.4)
MDAAT, 2005 version	-14.6 (± 75.2)	-14.7 (± 68.7)	0.8 (± 69.4)	-34.8 (± 47.5)
Muscle enzymes	-19.8 (± 24.1)	8.7 (± 44.2)	-3.9 (± 42.6)	-8.3 (± 50.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change in CDASI From Start to End of Zetomipzomib (KZR-616) Treatment

End point title	Mean Change in CDASI From Start to End of Zetomipzomib (KZR-616) Treatment
End point description: Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) is a clinician scored single-page instrument that separately measures activity and damage, which consists of three (3) activity measures and two (2) damage measures which are assessed over 15 body areas. Scores range from 0-100 for activity and from 0-32 for damage, with higher scores indicating more severe disease.	
End point type	Secondary
End point timeframe: 32 weeks	

End point values	Arm A: Period 1 (Zetomipzomib)	Arm B: Period 1 (Placebo)	Arm A: Period 2 (Placebo)	Arm B: Period 2 (Zetomipzomib)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5 ^[2]	6 ^[3]	5 ^[4]	6 ^[5]
Units: score on a scale				
arithmetic mean (standard deviation)				
Activity score	-2.2 (± 5.3)	-1.2 (± 13.5)	-4.4 (± 5.2)	-0.2 (± 16.1)
Damage score	0.0 (± 0.7)	-0.8 (± 2.1)	-0.2 (± 0.8)	-1.7 (± 3.1)

Notes:

[2] - This measure was only performed for patients with DM.

[3] - This measure was only performed for patients with DM.

[4] - This measure was only performed for patients with DM.

[5] - This measure was only performed for patients with DM.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change in PP-NRS From Start to End of Zetomipzomib (KZR-616) Treatment

End point title	Mean Change in PP-NRS From Start to End of Zetomipzomib (KZR-616) Treatment
End point description: The Peak Pruritus Numeric Rating Scale (PP-NRS) is used to evaluate severity of itch in DM patients. Scores range from 0-10, with zero (0) representing no itch and ten (10) representing the worst itch imaginable within a 24-hour recall period.	
End point type	Secondary

End point timeframe:

32 weeks

End point values	Arm A: Period 1 (Zetomipzomib)	Arm B: Period 1 (Placebo)	Arm A: Period 2 (Placebo)	Arm B: Period 2 (Zetomipzomib)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5 ^[6]	6 ^[7]	5 ^[8]	6 ^[9]
Units: score on a scale				
arithmetic mean (standard deviation)	-1.8 (± 1.3)	-2.0 (± 4.2)	-2.0 (± 1.9)	-3.5 (± 3.5)

Notes:

[6] - This measure was only performed for patients with DM.

[7] - This measure was only performed for patients with DM.

[8] - This measure was only performed for patients with DM.

[9] - This measure was only performed for patients with DM.

Statistical analyses

No statistical analyses for this end point

Secondary: PK of Zetomipzomib [KZR-616] (Cmax)

End point title	PK of Zetomipzomib [KZR-616] (Cmax)
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End point description:

This is the maximum observed plasma concentration (Cmax) observed after administration of the first dose of KZR-616 (either Week 0 or Week 16). The pharmacokinetic (PK) parameters were calculated using all timepoints at which the concentration was measured, ie. pre-dose and 30 minutes, and 4 hours post-dose, with an additional sample obtained at 0.25, 1, or 2 hours post-dose.

End point type	Secondary
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End point timeframe:

4 hours

End point values	Zetomipzomib First, Then Placebo (Arm A)	Placebo First, Then Zetomipzomib (Arm B)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	12		
Units: ng/mL				
geometric mean (geometric coefficient of variation)	57.5 (± 78.9)	82.3 (± 42.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK of Zetomipzomib [KZR-616] (Tmax)

End point title	PK of Zetomipzomib [KZR-616] (Tmax)
End point description:	
This is the time to maximum observed plasma concentration (tmax) observed after administration of the first dose of KZR-616 (either Week 0 or Week 16). The PK parameters were calculated using all timepoints at which the concentration was measured, ie. predose and 30 minutes, and 4 hours postdose, with an additional sample obtained at 0.25, 1, or 2 hours postdose.	
End point type	Secondary
End point timeframe:	
4 hours	

End point values	Zetomipzomib First, Then Placebo (Arm A)	Placebo First, Then Zetomipzomib (Arm B)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	12		
Units: hours				
geometric mean (full range (min-max))	0.50 (0.25 to 0.53)	0.50 (0.25 to 0.55)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK of Zetomipzomib [KZR-616] (AUC)

End point title	PK of Zetomipzomib [KZR-616] (AUC)
End point description:	
This is the area under the curve (AUC) from predose through 4 hour postdose observed after administration of the first dose of KZR-616 (either Week 0 or Week 16). The PK parameters were calculated using all timepoints at which the concentration was measured, ie. predose and 30 minutes, and 4 hours postdose, with an additional sample obtained at 0.25, 1, or 2 hours postdose.	
End point type	Secondary
End point timeframe:	
4 hours	

End point values	Zetomipzomib First, Then Placebo (Arm A)	Placebo First, Then Zetomipzomib (Arm B)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	12		
Units: ng*h/mL				
geometric mean (geometric coefficient of variation)	120 (\pm 59.0)	156 (\pm 40.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK of KZR-59587 (Cmax)

End point title	PK of KZR-59587 (Cmax)
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End point description:

This is the maximum observed plasma concentration of KZR-59587 (Cmax) observed after administration of the first dose of KZR-616 (either Week 0 or Week 16). The pharmacokinetic (PK) parameters were calculated using all timepoints at which the concentration was measured, ie. pre-dose and 30 minutes, and 4 hours post-dose, with an additional sample obtained at 0.25, 1, or 2 hours post-dose.

End point type	Secondary
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End point timeframe:

4 hours

End point values	Zetomipzomib First, Then Placebo (Arm A)	Placebo First, Then Zetomipzomib (Arm B)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	12		
Units: ng/mL				
geometric mean (geometric coefficient of variation)	48.2 (± 58.5)	58.5 (± 46.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK of KZR-59587 (Tmax)

End point title	PK of KZR-59587 (Tmax)
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End point description:

This is the time to maximum observed plasma concentration of KZR-59587 (tmax) observed after administration of the first dose of KZR-616 (either Week 0 or Week 16). The PK parameters were calculated using all timepoints at which the concentration was measured, ie. predose and 30 minutes, and 4 hours postdose, with an additional sample obtained at 0.25, 1, or 2 hours postdose.

End point type	Secondary
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End point timeframe:

4 hours

End point values	Zetomipzomib First, Then Placebo (Arm A)	Placebo First, Then Zetomipzomib (Arm B)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	12		
Units: hours				
geometric mean (full range (min-max))	2.50 (0.52 to 4.02)	3.92 (0.98 to 4.55)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK of KZR-59587 (AUC)

End point title	PK of KZR-59587 (AUC)
End point description:	
This is the area under the curve of KZR-59587 (AUC) from predose through 4 hour postdose observed after administration of the first dose of KZR-616 (either Week 0 or Week 16). The PK parameters were calculated using all timepoints at which the concentration was measured, ie. predose and 30 minutes, and 4 hours postdose, with an additional sample obtained at 0.25, 1, or 2 hours postdose.	
End point type	Secondary
End point timeframe:	
4 hours	

End point values	Zetomipzomib First, Then Placebo (Arm A)	Placebo First, Then Zetomipzomib (Arm B)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	12		
Units: ng*h/mL				
geometric mean (geometric coefficient of variation)	150 (\pm 59.2)	176 (\pm 53.3)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 40 weeks

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	25.1
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Reporting groups

Reporting group title	Arm A: Period 1 (Zetomipzomib)
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Reporting group description:

Zetomipzomib 30 mg SC weekly for 2 weeks, then 45 mg SC weekly for 14 weeks

Reporting group title	Arm A: Period 2 (Placebo)
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Reporting group description:

Placebo SC weekly for 16 weeks

Reporting group title	Arm B: Period 1 (Placebo)
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Reporting group description:

Placebo SC weekly for 16 weeks

Reporting group title	Arm B: Period 2 (Zetomipzomib)
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Reporting group description:

Zetomipzomib 30 mg SC weekly for 2 weeks, then 45 mg SC weekly for 14 weeks

Serious adverse events	Arm A: Period 1 (Zetomipzomib)	Arm A: Period 2 (Placebo)	Arm B: Period 1 (Placebo)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	1 / 12 (8.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinal detachment			

subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Arm B: Period 2 (Zetomipzomib)		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 12 (8.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Retinal detachment			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Arm A: Period 1 (Zetomipzomib)	Arm A: Period 2 (Placebo)	Arm B: Period 1 (Placebo)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 13 (92.31%)	8 / 10 (80.00%)	7 / 12 (58.33%)
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
General disorders and administration site conditions			
Chills			
subjects affected / exposed	2 / 13 (15.38%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	12	0	0
Fatigue			
subjects affected / exposed	5 / 13 (38.46%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	40	0	0
Feeling cold			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Feeling hot			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Influenza like illness			
subjects affected / exposed	1 / 13 (7.69%)	1 / 10 (10.00%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Injection site bruising			
subjects affected / exposed	1 / 13 (7.69%)	1 / 10 (10.00%)	0 / 12 (0.00%)
occurrences (all)	7	1	0
Injection site discomfort			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Injection site erythema			
subjects affected / exposed	5 / 13 (38.46%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	13	0	0
Injection site induration			

subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Injection site inflammation			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Injection site mass			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Injection site pain			
subjects affected / exposed	6 / 13 (46.15%)	0 / 10 (0.00%)	1 / 12 (8.33%)
occurrences (all)	32	0	2
Injection site pruritus			
subjects affected / exposed	2 / 13 (15.38%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	9	0	0
Injection site rash			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Injection site reaction			
subjects affected / exposed	3 / 13 (23.08%)	0 / 10 (0.00%)	2 / 12 (16.67%)
occurrences (all)	31	0	4
Injection site streaking			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Injection site swelling			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	6	0	0
Injection site vesicles			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	4 / 13 (30.77%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	24	0	0
Pyrexia			

subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 17	0 / 10 (0.00%) 0	0 / 12 (0.00%) 0
Vaccination site inflammation subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 10 (0.00%) 0	0 / 12 (0.00%) 0
Vaccination site reaction subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 10 (10.00%) 1	0 / 12 (0.00%) 0
Injection site nodule subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 6	0 / 10 (0.00%) 0	0 / 12 (0.00%) 0
Immune system disorders Food allergy subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 10 (0.00%) 0	1 / 12 (8.33%) 1
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 2	0 / 10 (0.00%) 0	0 / 12 (0.00%) 0
Pulmonary mass subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 10 (0.00%) 0	0 / 12 (0.00%) 0
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 10 (0.00%) 0	1 / 12 (8.33%) 1
Insomnia subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 10 (0.00%) 0	1 / 12 (8.33%) 1
Investigations Biopsy subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 10 (0.00%) 0	0 / 12 (0.00%) 0
Electrocardiogram QT prolonged subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 10 (0.00%) 0	0 / 12 (0.00%) 0

Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
QRS axis abnormal			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 13 (7.69%)	1 / 10 (10.00%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Hand fracture			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Muscle contusion			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Procedural pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Wound complication			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Wound secretion			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Post procedural pruritus			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Post vaccination syndrome			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Sinus tachycardia			

subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 2	0 / 10 (0.00%) 0	0 / 12 (0.00%) 0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Dizziness exertional			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	4 / 13 (30.77%)	0 / 10 (0.00%)	1 / 12 (8.33%)
occurrences (all)	13	0	1
Hypoaesthesia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Neuralgia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Post herpetic neuralgia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Somnolence			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Eye disorders			
Keratitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Vitreous detachment			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Gastrointestinal disorders			

Constipation			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	2 / 13 (15.38%)	0 / 10 (0.00%)	1 / 12 (8.33%)
occurrences (all)	3	0	1
Dyspepsia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Faeces discoloured			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Mouth ulceration			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	3 / 13 (23.08%)	1 / 10 (10.00%)	1 / 12 (8.33%)
occurrences (all)	7	1	1
Vomiting			
subjects affected / exposed	1 / 13 (7.69%)	1 / 10 (10.00%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Dermatomyositis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Mechanic's hand			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Panniculitis			

subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	3 / 13 (23.08%)	0 / 10 (0.00%)	1 / 12 (8.33%)
occurrences (all)	3	0	2
Rash			
subjects affected / exposed	3 / 13 (23.08%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	7	0	0
Skin discolouration			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Skin hyperpigmentation			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Proteinuria			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Urinary tract disorder			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 13 (15.38%)	0 / 10 (0.00%)	1 / 12 (8.33%)
occurrences (all)	2	0	2
Coccydynia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Joint swelling			

subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Limb discomfort			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Muscle twitching			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Muscular weakness			
subjects affected / exposed	2 / 13 (15.38%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Myalgia			
subjects affected / exposed	2 / 13 (15.38%)	1 / 10 (10.00%)	0 / 12 (0.00%)
occurrences (all)	8	1	0
Neck pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Osteoporosis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	1 / 13 (7.69%)	1 / 10 (10.00%)	0 / 12 (0.00%)
occurrences (all)	1	2	0
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 10 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Erythema migrans			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Eye infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0

Fungal skin infection subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 10 (0.00%) 0	0 / 12 (0.00%) 0
Gastroenteritis subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 10 (0.00%) 0	0 / 12 (0.00%) 0
Herpes zoster subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	2 / 10 (20.00%) 3	0 / 12 (0.00%) 0
Pharyngitis streptococcal subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 10 (0.00%) 0	0 / 12 (0.00%) 0
Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 10 (0.00%) 0	1 / 12 (8.33%) 1
Urinary tract infection subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 2	0 / 10 (0.00%) 0	3 / 12 (25.00%) 3
COVID-19 subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 10 (0.00%) 0	1 / 12 (8.33%) 1
Metabolism and nutrition disorders Iron deficiency subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 10 (0.00%) 0	0 / 12 (0.00%) 0

Non-serious adverse events	Arm B: Period 2 (Zetomipzomib)		
Total subjects affected by non-serious adverse events subjects affected / exposed	10 / 12 (83.33%)		
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
General disorders and administration site conditions Chills			

subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Feeling cold			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Feeling hot			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Influenza like illness			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Injection site bruising			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	14		
Injection site discomfort			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Injection site erythema			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	25		
Injection site induration			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	4		
Injection site inflammation			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Injection site mass			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Injection site pain			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Injection site pruritus			

subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	9		
Injection site rash			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Injection site reaction			
subjects affected / exposed	6 / 12 (50.00%)		
occurrences (all)	57		
Injection site streaking			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Injection site swelling			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Injection site vesicles			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Oedema peripheral			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Pain			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	3		
Vaccination site inflammation			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Vaccination site reaction			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Injection site nodule			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Immune system disorders			

Food allergy subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all) Pulmonary mass subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0 1 / 12 (8.33%) 1		
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0 0 / 12 (0.00%) 0		
Investigations Biopsy subjects affected / exposed occurrences (all) Electrocardiogram QT prolonged subjects affected / exposed occurrences (all) Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all) QRS axis abnormal subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0		
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all) Hand fracture	0 / 12 (0.00%) 0		

subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Muscle contusion			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Procedural pain			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Wound complication			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Wound secretion			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Post procedural pruritus			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Post vaccination syndrome			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Sinus tachycardia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Dizziness exertional			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Headache			

subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Hypoaesthesia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Neuralgia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Paraesthesia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Post herpetic neuralgia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Somnolence			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Eye disorders			
Keratitis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	3		
Vitreous detachment			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Faeces discoloured			

subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Mouth ulceration			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Dermatomyositis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Erythema			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Mechanic's hand			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Panniculitis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	3 / 12 (25.00%)		
occurrences (all)	4		
Rash			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Skin discolouration			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		

Skin hyperpigmentation subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Urticaria subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Proteinuria subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Urinary tract disorder subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Coccydynia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Joint swelling subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Limb discomfort subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Muscle spasms subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Muscle twitching subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Muscular weakness			

subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Neck pain			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Osteoporosis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Erythema migrans			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Eye infection			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Fungal skin infection			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Gastroenteritis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Herpes zoster			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Pharyngitis streptococcal			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		

Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Urinary tract infection subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
COVID-19 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Metabolism and nutrition disorders Iron deficiency subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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.

Study was not powered to detect statistical differences between treatment arms. Crossover study design with no washout period may have confounded assessments. Limited information from safety follow-up as most patients elected to join the OLE study.
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Notes: