



Clinical trial results:

A Randomized, Double-blind, Placebo-controlled, Dose Ranging Phase 2 Study to Evaluate the Efficacy and Safety of RIST4721 in Subjects with Palmoplantar Pustulosis

Summary

EudraCT number	2021-003029-31
Trial protocol	DE CZ HU
Global end of trial date	06 March 2023

Results information

Result version number	v1 (current)
This version publication date	30 June 2023
First version publication date	30 June 2023

Trial information

Trial identification

Sponsor protocol code	RIST4721-202
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05194839
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Aristea Therapeutics Inc.
Sponsor organisation address	12770 High Bluff Drive, San Diego, United States, 92130
Public contact	Aristea Therapeutics Inc., Aristea Therapeutics Inc., +1 858-465-6142, info@aristeatx.com
Scientific contact	Aristea Therapeutics Inc., Aristea Therapeutics Inc., +1 858-465-6142, info@aristeatx.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	06 March 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 February 2023
Global end of trial reached?	Yes
Global end of trial date	06 March 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of RIST4721 in the treatment of subjects with moderate to severe PPP

Protection of trial subjects:

This study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practice (GCP) and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 January 2022
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	Poland: 10
Country: Number of subjects enrolled	Czechia: 8
Country: Number of subjects enrolled	Germany: 33
Country: Number of subjects enrolled	Hungary: 8
Country: Number of subjects enrolled	United States: 13
Country: Number of subjects enrolled	Canada: 7
Worldwide total number of subjects	79
EEA total number of subjects	59

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)	63
From 65 to 84 years	16
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects must have at least a 6-month history of PPP and have moderate or severe PPP.

Period 1

Period 1 title	Blinded Treatment Period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
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Arm title	RIST4721 400mg
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	RIST4721
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

RIST4721 tablets, 100 mg (4 x 100 mg tablet) once daily.

Arm title	RIST4721 200mg
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	RIST4721
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

RIST4721 tablets, 100 mg (2 x 100 mg tablet and 2 placebo tablets) once daily.

Arm title	Placebo
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Arm description: -

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

Dosage and administration details:

Placebo (4 placebo tablets) once daily.

Number of subjects in period 1	RIST4721 400mg	RIST4721 200mg	Placebo
Started	27	26	26
Completed	12	13	12
Not completed	15	13	14
Consent withdrawn by subject	2	1	1
Adverse event, non-fatal	2	2	1
Other	-	-	1
Study Terminated by Sponsor	11	10	11

Baseline characteristics

Reporting groups

Reporting group title	RIST4721 400mg
Reporting group description: -	
Reporting group title	RIST4721 200mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	RIST4721 400mg	RIST4721 200mg	Placebo
Number of subjects	27	26	26
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	21	22	20
From 65-84 years	6	4	6
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	23	23	19
Male	4	3	7

Reporting group values	Total		
Number of subjects	79		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	63		
From 65-84 years	16		
85 years and over	0		
Gender categorical			
Units: Subjects			
Female	65		
Male	14		

End points

End points reporting groups

Reporting group title	RIST4721 400mg
Reporting group description: -	
Reporting group title	RIST4721 200mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Subject analysis set title	RIST4721 400mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects who completed Week 12	
Subject analysis set title	RIST4721 200mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects who completed Week 12	
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects who completed Week 12	

Primary: Proportion of Subjects Achieving 50% Reduction in PPPASI Score at Week 12

End point title	Proportion of Subjects Achieving 50% Reduction in PPPASI Score at Week 12 ^[1]
End point description:	
End point type	Primary
End point timeframe:	
From baseline to Week 12	

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 formal statistical hypothesis testing was conducted due to early study termination. Descriptive statistics were used to summarize the primary endpoint.

End point values	RIST4721 400mg	RIST4721 200mg	Placebo	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	12	13	12	
Units: Number of Subjects	6	3	5	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline through end of Week 12 (blinded treatment) and follow-up.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	24.1
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Reporting groups

Reporting group title	RIST4721 400mg
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Reporting group description: -

Reporting group title	RIST4721 200mg
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Reporting group description: -

Reporting group title	Placebo
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Reporting group description: -

Serious adverse events	RIST4721 400mg	RIST4721 200mg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatic lesion			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	RIST4721 400mg	RIST4721 200mg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 27 (66.67%)	17 / 26 (65.38%)	18 / 26 (69.23%)

Vascular disorders Hypertension subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 2	0 / 26 (0.00%) 0	1 / 26 (3.85%) 1
Surgical and medical procedures Tooth extraction subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	1 / 26 (3.85%) 1	0 / 26 (0.00%) 0
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all) Xerosis subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1 1 / 27 (3.70%) 1 0 / 27 (0.00%) 0	1 / 26 (3.85%) 1 0 / 26 (0.00%) 0 0 / 26 (0.00%) 0	1 / 26 (3.85%) 1 0 / 26 (0.00%) 0 1 / 26 (3.85%) 1
Reproductive system and breast disorders Ovarian cyst subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1	0 / 26 (0.00%) 0	0 / 26 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Bronchitis subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1 0 / 27 (0.00%) 0 0 / 27 (0.00%) 0	0 / 26 (0.00%) 0 0 / 26 (0.00%) 0 0 / 26 (0.00%) 0	0 / 26 (0.00%) 0 1 / 26 (3.85%) 1 1 / 26 (3.85%) 1
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	2 / 26 (7.69%) 2	0 / 26 (0.00%) 0

Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	1 / 26 (3.85%) 1	0 / 26 (0.00%) 0
C-reactive protein increased subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 2	0 / 26 (0.00%) 0	0 / 26 (0.00%) 0
Hepatic enzyme increased subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	2 / 26 (7.69%) 2	0 / 26 (0.00%) 0
Urine leukocyte esterase positive subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 26 (0.00%) 0	1 / 26 (3.85%) 1
Weight decreased subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1	0 / 26 (0.00%) 0	0 / 26 (0.00%) 0
White blood cell count increased subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1	0 / 26 (0.00%) 0	0 / 26 (0.00%) 0
Injury, poisoning and procedural complications Ligament rupture subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 26 (0.00%) 0	1 / 26 (3.85%) 1
Cardiac disorders Bundle branch block left subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 26 (0.00%) 0	1 / 26 (3.85%) 1
Nervous system disorders Dysaesthesia subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 26 (0.00%) 0	1 / 26 (3.85%) 1
Headache subjects affected / exposed occurrences (all)	3 / 27 (11.11%) 3	1 / 26 (3.85%) 1	1 / 26 (3.85%) 1
Vertigo subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1	0 / 26 (0.00%) 0	0 / 26 (0.00%) 0

Blood and lymphatic system disorders	Anaemia macrocytic			
	subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	0 / 26 (0.00%)
	occurrences (all)	1	0	0
	Neutropenia			
Eye disorders	subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	0 / 26 (0.00%)
	occurrences (all)	1	0	0
	Blepharitis			
	subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
Gastrointestinal disorders	occurrences (all)	0	1	0
	Vision blurred			
	subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
	occurrences (all)	0	1	0
Gastrointestinal disorders	Abdominal pain			
	subjects affected / exposed	2 / 27 (7.41%)	0 / 26 (0.00%)	0 / 26 (0.00%)
	occurrences (all)	2	0	0
	Abnormal faeces			
	subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
	occurrences (all)	0	1	0
	Constipation			
	subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
	occurrences (all)	0	1	0
	Diarrhoea			
	subjects affected / exposed	4 / 27 (14.81%)	1 / 26 (3.85%)	0 / 26 (0.00%)
	occurrences (all)	4	1	0
	Dry mouth			
	subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
	occurrences (all)	0	1	0
	Flatulence			
	subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
	occurrences (all)	0	1	0
	Haemorrhoids			
	subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	0 / 26 (0.00%)
	occurrences (all)	1	0	0
	Inguinal hernia			

subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 26 (0.00%) 0	1 / 26 (3.85%) 1
Nausea subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1	1 / 26 (3.85%) 1	0 / 26 (0.00%) 0
Vomiting subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 0	0 / 26 (0.00%) 0	0 / 26 (0.00%) 0
Skin and subcutaneous tissue disorders			
Diffuse alopecia subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 26 (0.00%) 0	1 / 26 (3.85%) 1
Hand dermatitis subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 26 (0.00%) 0	1 / 26 (3.85%) 1
Palmoplantar pustulosis subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	1 / 26 (3.85%) 1	0 / 26 (0.00%) 0
Petechiae subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 26 (0.00%) 0	1 / 26 (3.85%) 1
Pruritus subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 26 (0.00%) 0	1 / 26 (3.85%) 1
Psoriasis subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1	0 / 26 (0.00%) 0	1 / 26 (3.85%) 1
Renal and urinary disorders			
Haematuria subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1	0 / 26 (0.00%) 0	0 / 26 (0.00%) 0
Urine odor abnormal subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1	3 / 26 (11.54%) 3	0 / 26 (0.00%) 0
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Back pain			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	2
Invertebral disc protrusion			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Neck pain			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Asymptomatic COVID-19			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Asymptomatic bacteriuria			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Bacterial vaginosis			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Bronchitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
COVID-19			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
Cystitis bacterial			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Fungal skin infection			

subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Furuncle			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	1 / 27 (3.70%)	3 / 26 (11.54%)	4 / 26 (15.38%)
occurrences (all)	1	3	4
Periodontitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Respiratory tract infection			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Tonsillitis			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
Urinary tract infection			
subjects affected / exposed	1 / 27 (3.70%)	1 / 26 (3.85%)	1 / 26 (3.85%)
occurrences (all)	1	1	1
Viral diarrhoea			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 November 2021	The primary purpose of this amendment was to provide additional guidance/clarification regarding the SARs-CoV-2 vaccine and inclusion criteria regarding SARs-CoV-2 vaccination, to amend contact in case of SAE/pregnancy if the electronic system is not available, and other minor edits and clarifications.
05 April 2022	The primary purpose of this amendment was to incorporate open-label extension as well as other minor edits and clarifications.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
13 January 2023	Study RIST4721-202 was terminated due to safety findings.	-

Notes:

Limitations and caveats

None reported