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

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
Arm title	RIST4721 400mg

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

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

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
Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.1
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: -	

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

Aspartate aminotransferase increased			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
C-reactive protein increased			
subjects affected / exposed	2 / 27 (7.41%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	2	0	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 27 (0.00%)	2 / 26 (7.69%)	0 / 26 (0.00%)
occurrences (all)	0	2	0
Urine leukocyte esterase positive			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Weight decreased			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
White blood cell count increased			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Ligament rupture			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Cardiac disorders			
Bundle branch block left			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Nervous system disorders			
Dysaesthesia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	3 / 27 (11.11%)	1 / 26 (3.85%)	1 / 26 (3.85%)
occurrences (all)	3	1	1
Vertigo			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	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			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Blepharitis			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
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	0 / 27 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	1 / 27 (3.70%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	1	1	0
Vomiting			
subjects affected / exposed	2 / 27 (7.41%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Diffuse alopecia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Hand dermatitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Palmoplantar pustulosis			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Petechiae			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Psoriasis			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Urine odor abnormal			
subjects affected / exposed	1 / 27 (3.70%)	3 / 26 (11.54%)	0 / 26 (0.00%)
occurrences (all)	1	3	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