Clinical trial results:
A Phase 2, Double Blind, Placebo Controlled Study of RSLV-132 in Subjects with Primary Sjogren's Syndrome

Summary

EudraCT number	2016-001586-87
Trial protocol	GB
Global end of trial date	28 August 2018

Results information

Result version number	v1 (current)
This version publication date	17 December 2020
First version publication date	17 December 2020

Trial information

Trial identification

Sponsor protocol code	RSLV-132-04

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03247686
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Resolve Therapeutics LLC
Sponsor organisation address	721 1st Avenue North , St. Petersburg, FL 33701, United States,
Public contact	Chief Executive Officer, Resolve Therapeutics, LLC, 001 208727 7010, jp@resolvebio.com
Scientific contact	Chief Executive Officer, Resolve Therapeutics, LLC, 2087277010 208727 7010, jp@resolvebio.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	02 November 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 August 2018
Global end of trial reached?	Yes
Global end of trial date	28 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary endpoint of the study is to assess changes in blood cell gene expression or serum protein levels indicative of reduced inflammation in the active versus control groups.

Protection of trial subjects:

Standard procedures for emergency care were followed for any individual adverse events if clinically needed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 September 2016
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 Kingdom: 28
Worldwide total number of subjects	28
EEA total number of subjects	28

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)	20
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Potential participant were screened to assess their eligibility within 60 days prior to study entry. Eligible participants were randomized in a 3:1 ratio to either RSLV-132 or placebo. A total of 22 participants were randomised to RSLV-2 and 8 to placebo. Two participants randomized to RSLV-2 were withdrawn prior to the start of study treatment.

Period 1

Period 1 title	Overall study (overall period)
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?	Yes
Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous drip use

Dosage and administration details:

Placebo was administered as an IV infusion with an initial infusion rate of 167 mL/hour and over approximately 90 minutes.

Arm title	RSLV-132

Arm description: -

Arm type	Experimental
Investigational medicinal product name	RSLV-132
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous drip use

Dosage and administration details:

RSLV-132 was administered as IV infusions with an initial infusion rate of 167 mL/hour and over approximately 90 minutes.

Number of subjects in period 1	Placebo	RSLV-132
Started	8	20
Completed	7	18
Not completed	1	2
Consent withdrawn by subject	1	2

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	RSLV-132
Reporting group description: -	

Reporting group values	Placebo	RSLV-132	Total
Number of subjects	8	20	28
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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	59.6	56.5	
standard deviation	± 8.8	± 12.9	-
Gender categorical Units: Subjects			
Female	8	20	28
Male	0	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	0	1	1
Not Hispanic or Latino	8	19	27
Unknown or Not Reported	0	0	0
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	1	2
Native Hawaiian or other Pacific Islander	0	0	0
White	7	19	26
More than One Race	0	0	0
Unknown or Not Reported	0	0	0
Black or African American	0	0	0
EULAR Sjogren's Syndrome Disease Activity Index (ESSDAI) Total Score Units: total score			
arithmetic mean	5.1	5.0	

standard deviation	± 4.1	± 4.6	-

End points

End points reporting groups	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	RSLV-132
Reporting group description: -	

Primary: Blood Cell Gene Expression	
End point title	Blood Cell Gene Expression
End point description:	
End point type	Primary
End point timeframe:	
Day 99	

End point values	Placebo	RSLV-132		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	20		
Units: log2 fold change from baseline				
arithmetic mean (standard error)				
Module M1.2	-0.0291486 (± 0.1151235)	0.1330903 (± 0.09136563)		
Module M3.4	-0.0301788 (± 0.1362689)	0.08489987 (± 0.08673372)		
Module M5.12	-0.0572555 (± 0.09889587)	0.02757946 (± 0.1279434)		

Statistical analyses

Statistical analysis title	Module M1.2 Placebo versus RSLV-132 All
Comparison groups	Placebo v RSLV-132
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.00005
Method	t-test, 2-sided

Statistical analysis title	Module M3.4 Placebo versus RSLV-132 All
Comparison groups	Placebo v RSLV-132

Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.00001
Method	t-test, 2-sided

Statistical analysis title	Module 5.12 Placebo versus RSLV-132 All
Comparison groups	Placebo v RSLV-132
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.00044
Method	t-test, 2-sided

Secondary: EULAR ESSDAI Total Score

End point title	EULAR ESSDAI Total Score
End point description:	

End point type	Secondary
End point timeframe:	
Day 99	

End point values	Placebo	RSLV-132		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	20		
Units: Change from Baseline in Total Score				
arithmetic mean (standard deviation)	-2.5 (± 4.3)	0.0 (± 3.8)		

Statistical analyses

Statistical analysis title	Mean difference in Change from Baseline (95% CI)
Comparison groups	Placebo v RSLV-132
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	equivalence[1]
P-value	= 0.18
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-2.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.34
upper limit	1.34

Notes:

[1] - Two sample t-test with Satterthwaite approximation

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From screening until Day 211	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.1
Reporting groups	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	RSLV-132
Reporting group description: -	

Serious adverse events	Placebo	RSLV-132	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	1 / 20 (5.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Infections and infestations			
Parotitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Placebo	RSLV-132	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 8 (100.00%)	20 / 20 (100.00%)	
General disorders and administration site conditions			
Catheter site erythema			
subjects affected / exposed	1 / 8 (12.50%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	1 / 8 (12.50%)	6 / 20 (30.00%)	
occurrences (all)	1	7	

Oedema peripheral			
subjects affected / exposed	1 / 8 (12.50%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 8 (12.50%)	2 / 20 (10.00%)	
occurrences (all)	1	2	
Oropharyngeal pain			
subjects affected / exposed	0 / 8 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	2	
Psychiatric disorders			
Mood altered			
subjects affected / exposed	1 / 8 (12.50%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Sleep disorder			
subjects affected / exposed	1 / 8 (12.50%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Investigations			
Weight increased			
subjects affected / exposed	0 / 8 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	2	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 8 (12.50%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Head injury			
subjects affected / exposed	1 / 8 (12.50%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Infusion related reaction			
subjects affected / exposed	1 / 8 (12.50%)	1 / 20 (5.00%)	
occurrences (all)	2	1	
Joint injury			
subjects affected / exposed	1 / 8 (12.50%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Thermal burn			

subjects affected / exposed	1 / 8 (12.50%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 8 (12.50%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Palpitations			
subjects affected / exposed	1 / 8 (12.50%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 8 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	2	
Headache			
subjects affected / exposed	1 / 8 (12.50%)	3 / 20 (15.00%)	
occurrences (all)	1	4	
Presyncope			
subjects affected / exposed	1 / 8 (12.50%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Sensorimotor disorder			
subjects affected / exposed	1 / 8 (12.50%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Tremor			
subjects affected / exposed	1 / 8 (12.50%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	1 / 8 (12.50%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	1 / 8 (12.50%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Conjunctival hyperaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Eye pain			

subjects affected / exposed	1 / 8 (12.50%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 8 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	2	
Diarrhoea			
subjects affected / exposed	1 / 8 (12.50%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Dyspepsia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Hiatus hernia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Mouth ulceration			
subjects affected / exposed	1 / 8 (12.50%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Nausea			
subjects affected / exposed	1 / 8 (12.50%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Vomiting			
subjects affected / exposed	1 / 8 (12.50%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	0 / 8 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	3	
Rash			
subjects affected / exposed	0 / 8 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	2	
Rash papular			
subjects affected / exposed	0 / 8 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	2	
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	0 / 8 (0.00%)	5 / 20 (25.00%)	
occurrences (all)	0	5	
Joint swelling			
subjects affected / exposed	1 / 8 (12.50%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Limb discomfort			
subjects affected / exposed	1 / 8 (12.50%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Muscle spasms			
subjects affected / exposed	1 / 8 (12.50%)	2 / 20 (10.00%)	
occurrences (all)	1	2	
Osteoarthritis			
subjects affected / exposed	1 / 8 (12.50%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Pain in extremity			
subjects affected / exposed	1 / 8 (12.50%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Palindromic rheumatism			
subjects affected / exposed	1 / 8 (12.50%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Sjogren's syndrome			
subjects affected / exposed	2 / 8 (25.00%)	0 / 20 (0.00%)	
occurrences (all)	3	0	
Tendonitis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	1 / 8 (12.50%)	3 / 20 (15.00%)	
occurrences (all)	1	4	
Gastroenteritis viral			
subjects affected / exposed	1 / 8 (12.50%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Hordeolum			

subjects affected / exposed	1 / 8 (12.50%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Lower respiratory tract infection			
subjects affected / exposed	3 / 8 (37.50%)	1 / 20 (5.00%)	
occurrences (all)	3	1	
Parotitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	0 / 8 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	3	
Viral infection			
subjects affected / exposed	1 / 8 (12.50%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 8 (12.50%)	4 / 20 (20.00%)	
occurrences (all)	1	6	
Upper respiratory tract infection			
subjects affected / exposed	2 / 8 (25.00%)	5 / 20 (25.00%)	
occurrences (all)	3	8	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 8 (12.50%)	0 / 20 (0.00%)	
occurrences (all)	1	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

None reported