Clinical trial results:
A multi-center, randomized, participant- and investigator- blinded, placebo-controlled, parallel group basket study to evaluate the safety, tolerability and efficacy of MHV370 in participants with Sjögren's Syndrome or Mixed Connective Tissue Disease

Summary

EudraCT number	2020-004937-19
Trial protocol	DE ES HU
Global end of trial date	07 March 2023

Results information

Result version number	v1 (current)
This version publication date	01 February 2024
First version publication date	01 February 2024

Trial information

Trial identification

Sponsor protocol code	CMHV370A12201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04988087
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.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	07 March 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 March 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of the trial were:
- To evaluate the efficacy of MHV370 compared to placebo based on change from baseline in ESSDAI [EULAR (European League against Rheumatism) Sjogren's Syndrome Disease Activity Index] in SjS (Sjogren´s Syndrome) participants
- To evaluate the efficacy of MHV370 compared to placebo based on change from baseline in Physician Global Assessment (PhGA) in MCTD (Mixed Connective Tissue Disease) participants.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 November 2021
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	China: 2
Country: Number of subjects enrolled	Taiwan: 4
Country: Number of subjects enrolled	Germany: 9
Country: Number of subjects enrolled	Hungary: 5
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	Poland: 9
Worldwide total number of subjects	30
EEA total number of subjects	24

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)	28
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in 10 investigative sites in 6 countries/regions.

Pre-assignment

Screening details:

There was a screening period of up to 6 weeks to assess participants eligibility.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	MHV370 200mg - SjS

Arm description:

MHV370 200mg oral dose, twice daily. SjS participants.

Arm type	Experimental
Investigational medicinal product name	MHV370
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

MHV370 200 mg oral twice daily - SjS participants

Arm title	Placebo - SjS

Arm description:

Placebo oral dose, twice daily. SjS participants.

Arm type	Placebo
Investigational medicinal product name	MHV370
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Placebo oral twice daily - SjS participants

Arm title	MHV370 200mg - MCTD

Arm description:

MHV370 200mg oral dose, twice daily. MCTD participants.

Arm type	Experimental
Investigational medicinal product name	MHV370
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:
MHV370 200 mg oral twice daily - MCTD participants

Arm title	Placebo - MCTD

Arm description:
Placebo oral dose, twice daily. MCTD participants.

Arm type	Placebo
Investigational medicinal product name	MHV370
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:
Placebo oral twice daily - MCTD participants

Number of subjects in period 1	MHV370 200mg - SjS	Placebo - SjS	MHV370 200mg - MCTD
Started	12	14	2
Completed	0	4	1
Not completed	12	10	1
Consent withdrawn by subject	1	1	-
Adverse events	4	-	-
Technical problems	7	9	1

Number of subjects in period 1	Placebo - MCTD
Started	2
Completed	0
Not completed	2
Consent withdrawn by subject	-
Adverse events	-
Technical problems	2

Baseline characteristics

Reporting groups	
Reporting group title	MHV370 200mg - SjS
Reporting group description:	
MHV370 200mg oral dose, twice daily. SjS participants.	
Reporting group title	Placebo - SjS
Reporting group description:	
Placebo oral dose, twice daily. SjS participants.	
Reporting group title	MHV370 200mg - MCTD
Reporting group description:	
MHV370 200mg oral dose, twice daily. MCTD participants.	
Reporting group title	Placebo - MCTD
Reporting group description:	
Placebo oral dose, twice daily. MCTD participants.	

Reporting group values	MHV370 200mg - SjS	Placebo - SjS	MHV370 200mg - MCTD
Number of subjects	12	14	2
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)	11	13	2
From 65-84 years	1	1	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	49.3	54.7	35.0
standard deviation	± 12.20	± 9.67	± 12.73
Sex: Female, Male Units: participants			
Female	12	14	2
Male	0	0	0
Race/Ethnicity, Customized Units: Subjects			
Asian	3	3	0
White	9	11	2

Reporting group values	Placebo - MCTD	Total	
Number of subjects	2	30	
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)	2	28	
From 65-84 years	0	2	
85 years and over	0	0	
Age Continuous			
Units: years			
arithmetic mean	44.0		
standard deviation	± 0.00	-	
Sex: Female, Male			
Units: participants			
Female	2	30	
Male	0	0	
Race/Ethnicity, Customized			
Units: Subjects			
Asian	0	6	
White	2	24	

End points

End points reporting groups

Reporting group title	MHV370 200mg - SjS
Reporting group description: MHV370 200mg oral dose, twice daily. SjS participants.	
Reporting group title	Placebo - SjS
Reporting group description: Placebo oral dose, twice daily. SjS participants.	
Reporting group title	MHV370 200mg - MCTD
Reporting group description: MHV370 200mg oral dose, twice daily. MCTD participants.	
Reporting group title	Placebo - MCTD
Reporting group description: Placebo oral dose, twice daily. MCTD participants.	

Primary: SjS participants: Change from baseline in Eular Sjögren's Disease Activity Index (ESSDAI) after 24 weeks of treatment

End point title	SjS participants: Change from baseline in Eular Sjögren's Disease Activity Index (ESSDAI) after 24 weeks of treatment[1][2]
End point description: The ESSDAI is an established disease outcome measure for Sjögren's syndrome that classifies disease activity in 3-4 levels according to their severity (i.e., no, low, moderate, high), over each of 12 organ-specific domains. These scores are then summed across the 12 domains in a weighted manner to provide the total score. The score range is 0 - 123, where a higher ESSDAI score indicates more severe symptoms. A negative change score from baseline indicates improvement.	
End point type	Primary
End point timeframe: Baseline, Week 24	

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: Endpoint specific to and only reported for SjS participants

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint specific to and only reported for SjS participants

End point values	MHV370 200mg - SjS	Placebo - SjS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[3]	4		
Units: Score on scale				
arithmetic mean (standard error)	()	-4.39 (± 2.41)		

Notes:

[3] - The insufficient sampling scheme did not allow to provide the data.

Statistical analyses

No statistical analyses for this end point

Primary: MCTD participants: Change from baseline in physician's global assessment scale (PhGA) after 24 weeks of treatment

End point title	MCTD participants: Change from baseline in physician's global assessment scale (PhGA) after 24 weeks of treatment[4][5]

End point description:

The physician's global assessment scale is used for the Investigator to rate the disease activity of their patient using 100 mm visual analog scale (VAS) ranging from "no disease activity" (0) to "maximal disease activity" (100). A negative change score from baseline indicates improvement. Only participants with evaluable records are included.

End point type	Primary

End point timeframe:

Baseline, Week 24

Notes:

[4] - 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: Endpoint specific to and only reported for MCTD participants

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint specific to and only reported for MCTD participants

End point values	MHV370 200mg - MCTD	Placebo - MCTD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	0[6]		
Units: Score on scale				
median (full range (min-max))	-62.00 (-62.00 to -62.00)	(to)		

Notes:

[6] - The insufficient sampling scheme did not allow to provide the data.

Statistical analyses

No statistical analyses for this end point

Secondary: SjS and MCTD participants: Maximum observed plasma concentrations (Cmax) of MHV370 at steady state

End point title	SjS and MCTD participants: Maximum observed plasma concentrations (Cmax) of MHV370 at steady state[7]

End point description:

Cmax is the maximum (peak) observed plasma concentration of MHV370 after single dose administration. Pharmacokinetic (PK) parameters were calculated based on MHV370 plasma concentrations determined by a validated liquid chromatography and tandem mass spectrometry (LC-MS/MS) method with a lower limit of quantification of 1.0 ng/mL. Cmax was determined using non-compartmental methods. Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'.

End point type	Secondary

End point timeframe:

pre-dose, 0.5, 1, 2 ,4 and 6 hours after dosing at week 4

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK Endpoint not analyzed for participants on placebo

End point values	MHV370 200mg - SjS	MHV370 200mg - MCTD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	1		
Units: ng/mL				
arithmetic mean (standard deviation)	278 (± 85.7)	194 (± 999)		

Statistical analyses

No statistical analyses for this end point

Secondary: SjS and MCTD participants: Change from baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) scale

End point title	SjS and MCTD participants: Change from baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) scale

End point description:

The Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F v4) is a short, 13-item patient-reported measure, easy-to-administer tool that measures an individual's level of fatigue during their usual daily activities over the past week. The level of fatigue is measured on a 5-point Likert scale (0 = not at all, 1 = a little bit, 2 = somewhat, 3 = quite a bit, 4 = very much). To score the FACIT-fatigue, all items are summed to create a single fatigue score with a range from 0 to 52, where a higher FACIT-F score indicates more severe symptoms. A negative change score from baseline indicates improvement. Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'.
The Number of Subjects Analyzed differs as stated on the category column, in case of difference from Number of subjects that started the Arm.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12, 20 and 24

End point values	MHV370 200mg - SjS	Placebo - SjS	MHV370 200mg - MCTD	Placebo - MCTD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	12	2	1
Units: Score on scale				
arithmetic mean (standard deviation)				
Week 4	0.13 (± 3.271)	-1.58 (± 6.052)	15.50 (± 9.192)	-3.00 (± 999)
Week 8 (n= 7,10,2,1)	3.14 (± 5.928)	-2.80 (± 4.185)	20.00 (± 7.071)	-2.00 (± 999)
Week 12 (n= 4,7,1,0)	-1.25 (± 6.702)	2.71 (± 8.826)	20.00 (± 999)	999 (± 999)
Week 20 (n= 1,5,1,0)	-9.42 (± 999)	4.80 (± 8.758)	23.00 (± 999)	999 (± 999)
Week 24 (n= 0,4,1,0)	999 (± 999)	5.75 (± 10.782)	30.00 (± 999)	999 (± 999)

Statistical analyses

No statistical analyses for this end point

Secondary: SjS and MCTD participants: Area under the plasma concentration-time curve from time zero to 6 hours (AUC0-6h) of MHV370

End point title	SjS and MCTD participants: Area under the plasma concentration-time curve from time zero to 6 hours (AUC0-6h) of MHV370[8]

End point description:

The AUC from time zero to the 6-hours post-dose sampling time. Pharmacokinetic (PK) parameters were calculated based on MHV370 plasma concentrations determined by a validated liquid chromatography and tandem mass spectrometry (LC-MS/MS) method with a lower limit of quantification of 1.0 ng/mL. AUClast was determined using non-compartmental methods. Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'.

End point type	Secondary

End point timeframe:

pre-dose, 0.5, 1, 2 ,4 and 6 hours after dosing at week 4

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK Endpoint not analyzed for participants on placebo

End point values	MHV370 200mg - SjS	MHV370 200mg - MCTD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	1		
Units: ng*h/mL				
arithmetic mean (standard deviation)	1060 (± 462)	742 (± 999)		

Statistical analyses

No statistical analyses for this end point

Secondary: SjS and MCTD participants: Time to reach maximum plasma concentrations (Tmax) of MHV370 at steady state

End point title	SjS and MCTD participants: Time to reach maximum plasma concentrations (Tmax) of MHV370 at steady state[9]

End point description:

Tmax is the time to reach maximum (peak) plasma concentration of MHV370 after single dose administration. Pharmacokinetic (PK) parameters were calculated based on MHV370 plasma concentrations determined by a validated liquid chromatography and tandem mass spectrometry (LC-MS/MS) method with a lower limit of quantification of 1.0 ng/mL. Tmax was determined using non-compartmental methods. Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'.

End point type	Secondary

End point timeframe:

pre-dose, 0.5, 1, 2 ,4 and 6 hours after dosing at week 4

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK Endpoint not analyzed for participants on placebo

End point values	MHV370 200mg - SjS	MHV370 200mg - MCTD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	1		
Units: hours				
median (full range (min-max))	1.50 (1.00 to 4.00)	2.00 (000 to 999)		

Statistical analyses

No statistical analyses for this end point

Secondary: SjS and MCTD participants: Change from baseline in Physician Global Assessment (PhGA)

End point title	SjS and MCTD participants: Change from baseline in Physician Global Assessment (PhGA)

End point description:

The physician’s global assessment scale is used for the Investigator to rate the disease activity of their patient using 100 mm visual analog scale (VAS) ranging from “no disease activity” (0) to “maximal disease activity” (100). A negative change score from baseline indicates improvement. Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating ‘not applicable’). Therefore, not applicable values are indicated as ‘999’.
The Number of Subjects Analyzed differs as stated on the category column, in case of difference from Number of subjects that started the Arm.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12, 20 and 24

End point values	MHV370 200mg - SjS	Placebo - SjS	MHV370 200mg - MCTD	Placebo - MCTD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	12	2	1
Units: Score on scale				
arithmetic mean (standard deviation)				
Week 4	-1.75 (± 12.658)	-5.25 (± 11.185)	-20.50 (± 12.021)	-15.00 (± 999)
Week 8 (n= 7,10,2,1)	2.57 (± 12.608)	-8.90 (± 11.474)	-39.00 (± 18.385)	-12.50 (± 999)
Week 12 (n= 4,7,1,0)	-4.00 (± 20.559)	-19.43 (± 14.328)	-66.00 (± 999)	999 (± 999)
Week 20 (n= 1,5,1,0)	3.00 (± 999)	-14.60 (± 22.423)	-64.00 (± 999)	999 (± 999)
Week 24 (n= 0,4,1,0)	999 (± 999)	-30.75 (± 19.534)	-62.00 (± 999)	999 (± 999)

Statistical analyses

No statistical analyses for this end point

Secondary: SjS participants: Change from baseline in Eular Sjögren's Syndrome Disease Activity Index (ESSDAI)

End point title	SjS participants: Change from baseline in Eular Sjögren's Syndrome Disease Activity Index (ESSDAI)[10]

End point description:

The ESSDAI is an established disease outcome measure for Sjögren's syndrome that classifies disease activity in 3-4 levels according to their severity (i.e., no, low, moderate, high), over each of 12 organ-specific domains. These scores are then summed across the 12 domains in a weighted manner to provide the total score. The score range is 0 - 123, where a higher ESSDAI score indicates more severe symptoms. A negative change score from baseline indicates improvement. Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'.
The Number of Subjects Analyzed differs as stated on the category column, in case of difference from Number of subjects that started the Arm.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12, 20 and 24

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint specific to and only reported for SjS participants

End point values	MHV370 200mg - SjS	Placebo - SjS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	12		
Units: Score on scale				
arithmetic mean (standard deviation)				
Week 4	-0.25 (± 1.753)	-3.67 (± 9.355)		
Week 8 (n= 7,10)	0.57 (± 6.528)	-4.80 (± 11.487)		
Week 12 (n= 3,7)	-3.00 (± 4.583)	-3.43 (± 7.656)		
Week 20 (n= 1,5)	-2.00 (± 999)	0.00 (± 14.629)		
Week 24 (n= 0,4)	999 (± 999)	-0.25 (± 11.117)		

Statistical analyses

No statistical analyses for this end point

Secondary: SjS participants: Change from baseline in Eular Sjögren's Syndrome Patient Reported Index (ESSPRI)

End point title	SjS participants: Change from baseline in Eular Sjögren's Syndrome Patient Reported Index (ESSPRI)[11]

End point description:

The ESSPRI is a disease outcome measure for Sjögren's syndrome. The ESSPRI is a patient-reported, subjective symptom index which consists of three questions covering the cardinal symptoms of Sjögren's syndrome: dryness, fatigue and pain (articular and/or muscular). The participant can assess severity of symptoms they experience on a single numerical scale of 0-10 (0=no symptom at all and 10= worst symptom imaginable) for each of the three domains. The overall score is calculated as the mean of the three individual domains where all domains carry the same weight. Min. score can be 0 and max. score can be 10, where a higher score indicates severe symptoms. A negative change score from baseline indicates improvement. Due to system limitations, data fields in the table cannot contain

letters. Therefore, not applicable values are indicated as '999'. The Number of Subjects Analyzed differs as stated on the category column, in case of difference from Number of subjects that started the Arm.

End point type	Secondary

End point timeframe:

baseline, weeks 4, 8, 12, 20 and 24

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint specific to and only reported for SjS participants

End point values	MHV370 200mg - SjS	Placebo - SjS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	12		
Units: Score on scale				
arithmetic mean (standard deviation)				
Week 4	-0.12 (± 0.354)	-0.53 (± 1.105)		
Week 8 (n= 7,10)	-0.67 (± 0.793)	-0.37 (± 1.511)		
Week 12 (n= 4,7)	-0.42 (± 0.500)	-1.38 (± 1.976)		
Week 20 (n= 1,5)	-0.17 (± 999)	-2.20 (± 1.865)		
Week 24 (n= 0,4)	999 (± 999)	-2.00 (± 2.000)		

Statistical analyses

No statistical analyses for this end point

Secondary: SjS participants: Change from baseline to the salivary flow rate

End point title	SjS participants: Change from baseline to the salivary flow

End point description:

Unstimulated whole salivary fluid secretions were collected over 5 minutes from participants. All assessments were performed at a fixed time of the day to minimize fluctuations related to the circadian rhythm of salivary flow and composition. Participants were instructed not to eat, drink or smoke for 90 minutes before the assessment. The start time and end time of saliva collection were recorded to calculate the salivary flow rate per minute. Only participants with evaluable records are included. Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'.
The Number of Subjects Analyzed differs as stated on the category column, in case of difference from Number of subjects that started the Arm.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 12 and 24

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint specific to and only reported for SjS participants

End point values	MHV370 200mg - SjS	Placebo - SjS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	14		
Units: mL/min				
arithmetic mean (standard deviation)				
Week 4	0.162 (± 0.2735)	-0.127 (± 0.7914)		
Week 12 (n= 4,7)	0.144 (± 0.2109)	0.183 (± 0.3944)		
Week 24 (n= 0,4)	999 (± 999)	0.564 (± 0.9193)		

Statistical analyses

No statistical analyses for this end point

Secondary: SjS participants: Change from baseline to the Schirmer's test

End point title	SjS participants: Change from baseline to the Schirmer's

End point description:

Schirmer's test is used to determine whether the eye produces enough tears to keep it moist especially for those who suffer from dry eye syndrome. A strip is placed in the lower eyelid for 5 minutes to assess tear production. After 5 minutes, the filter paper is removed and the distance between the leading edge of wetness and the initial fold is measured, using a millimeter ruler. Tear deficiency is defined as <5 mm wetting of the paper after 5 minutes. Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'.
The Number of Subjects Analyzed differs as stated on the category column, in case of difference from Number of subjects that started the Arm.

End point type	Secondary

End point timeframe:

Baseline, Week 4, 12 and 24

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint specific to and only reported for SjS participants

End point values	MHV370 200mg - SjS	Placebo - SjS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	14		
Units: milimeter				
arithmetic mean (standard deviation)				
Week 4, right eye (n= 8,12)	-1.5 (± 4.87)	0.0 (± 3.59)		
Week 12, right eye (n= 4,7)	-1.0 (± 2.16)	5.3 (± 8.81)		
Week 24, right eye (n= 0,4)	999 (± 999)	-3.0 (± 6.32)		
Week 4, left eye (n= 8,12)	1.1 (± 1.96)	1.6 (± 6.01)		
Week 12, left eye (n= 4,7)	2.0 (± 1.83)	4.9 (± 12.50)		
Week 24, left eye (n= 0,4)	999 (± 999)	-1.0 (± 2.94)		

Statistical analyses

No statistical analyses for this end point

Secondary: SjS participants: Sjögren's Tool for Assessing Response (STAR) response over time up to week 24

End point title	SjS participants: Sjögren's Tool for Assessing Response (STAR) response over time up to week 24[14]

End point description:

STAR is a composite responder index, including in a single tool all main disease features, and designed for use as a key efficacy endpoint in SjS Domain Point Definition of response.

Points are assigned in the following 5 domains, if the corresponding criteria are met:
- Systemic activity, if decrease in clin ESSDAI ≥ 3 points: 3 points
- Patient reported outcome, if decrease in ESSPRI ≥ 1 point or 15%: 3 points
- Lacrimal gland function (assessed by Schirmer's test), if abnormal score at baseline: increase ≥ 5 mm from baseline OR if normal score at baseline: no change to abnormal: 1 point
- Salivary gland function (assessed by unstimulated salivary flow), if increase ≥ 25% from baseline: 1 point
- Biological (assessed by serum IgG levels), if decrease ≥ 10%: 1 point

The Total Score is the sum of all 5 domain scores, ranging from 0 to 9 points. A STAR responder is defined as ≥ 5 points in the Total Score.

End point type	Secondary

End point timeframe:

Baseline, Week 4, 12 and 24

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint specific to and only reported for SjS participants

End point values	MHV370 200mg - SjS	Placebo - SjS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	14		
Units: participants				
Week 4	0	3		
Week 12	1	4		
Week 24	0	2		

Statistical analyses

No statistical analyses for this end point

Secondary: MCTD: Change from baseline in articular and pulmonary domains of the Eular Sjögren's Syndrome Disease Activity Index (ESSDAI)

End point title	MCTD: Change from baseline in articular and pulmonary domains of the Eular Sjögren's Syndrome Disease Activity Index (ESSDAI)[15]

End point description:

The ESSDAI is an established disease outcome measure for Sjögren's syndrome that classifies disease activity in 3-4 levels according to their severity (i.e., no, low, moderate, high), over each of 12 organ-specific domains. Participants with Mixed Connective Tissue Disease (MCTD) completed the articular (from 0 "no activity" to 3 "high activity") and pulmonary (from 0 "no activity to 3 "high activity") domains of the ESSDAI only. For MCTD participants, the score range is 0-21, where a higher score indicates more severe symptoms. A negative change score from baseline indicates improvement. Due to

EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'.
The Number of Subjects Analyzed differs as stated on the category column, in case of difference from Number of subjects that started the Arm.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12 and 24

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint specific to and only reported for MCTD participants

End point values	MHV370 200mg - MCTD	Placebo - MCTD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	1		
Units: Score on scale				
arithmetic mean (standard deviation)				
Week 4 - articular	0.00 (± 0.000)	0.00 (± 999)		
Week 8 - articular	-1.00 (± 0.000)	0.00 (± 999)		
Week 12 - articular (n= 1,0)	-1.00 (± 999)	999 (± 999)		
Week 24 - articular (n= 1,0)	-2.00 (± 999)	999 (± 999)		
Week 4 - pulmonary	0.00 (± 0.000)	0.00 (± 999)		
Week 8 - pulmonary	-0.50 (± 0.707)	0.00 (± 999)		
Week 12 - pulmonary (n= 1,0)	-1.00 (± 999)	999 (± 999)		
Week 24 - pulmonary (n= 1,0)	-1.00 (± 999)	999 (± 999)		

Statistical analyses

No statistical analyses for this end point

Secondary: MCTD participants: Change from baseline in Forced expiratory volume during the first three seconds (FEV3) of a forced breath

End point title	MCTD participants: Change from baseline in Forced expiratory volume during the first three seconds (FEV3) of a forced breath[16]

End point description:

FEV3 (forced expiratory volume in three seconds) is the amount of air which can be forcibly exhaled from the lungs in the first three seconds of a forced exhalation, measured through spirometry testing. A positive change from baseline in FEV3 is considered a favourable outcome. Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'.

End point type	Secondary

End point timeframe:

Baseline, Week 12

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint specific to and only reported for MCTD participants

End point values	MHV370 200mg - MCTD	Placebo - MCTD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	0[17]		
Units: liters (L)				
arithmetic mean (standard deviation)	0.460 (± 999)	()		

Notes:

[17] - The insufficient sampling scheme did not allow to provide the data.

Statistical analyses

No statistical analyses for this end point

Secondary: MCTD participants: Change from baseline in Forced expiratory volume during the first two seconds (FEV2) of a forced breath

End point title	MCTD participants: Change from baseline in Forced expiratory volume during the first two seconds (FEV2) of a forced breath[18]

End point description:

FEV2 (forced expiratory volume in two seconds) is the amount of air which can be forcibly exhaled from the lungs in the first two seconds of a forced exhalation, measured through spirometry testing. A positive change from baseline in FEV2 is considered a favourable outcome. Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'.

End point type	Secondary

End point timeframe:

Baseline, Week 12

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint specific to and only reported for MCTD participants

End point values	MHV370 200mg - MCTD	Placebo - MCTD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	0[19]		
Units: liters (L)				
arithmetic mean (standard deviation)	0.410 (± 999)	()		

Notes:

[19] - The insufficient sampling scheme did not allow to provide the data.

Statistical analyses

No statistical analyses for this end point

Secondary: MCTD participants: Change from baseline in Forced Vital Capacity (FVC)

End point title	MCTD participants: Change from baseline in Forced Vital Capacity (FVC)[20]

End point description:

Forced Vital Capacity (FVC) is the total amount of air exhaled during the Forced expiratory volume (FEV) test measured through spirometry testing. FEV measures how much air a person can exhale during a forced breath. A positive change from baseline is considered a favorable outcome. Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'.

End point type	Secondary

End point timeframe:

Baseline, Week 12

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint specific to and only reported for MCTD participants

End point values	MHV370 200mg - MCTD	Placebo - MCTD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	0[21]		
Units: liters (L)				
arithmetic mean (standard deviation)	0.530 (± 999)	()		

Notes:

[21] - The insufficient sampling scheme did not allow to provide the data.

Statistical analyses

No statistical analyses for this end point

Secondary: MCTD participants: Change from baseline in Forced expiratory volume during the first second (FEV1) of a forced breath

End point title	MCTD participants: Change from baseline in Forced expiratory volume during the first second (FEV1) of a forced breath[22]

End point description:

FEV1 (forced expiratory volume in one second) is the amount of air which can be forcibly exhaled from the lungs in the first second of a forced exhalation, measured through spirometry testing. A positive change from baseline in FEV1 is considered a favourable outcome. Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'.

End point type	Secondary

End point timeframe:

Baseline, Week 12

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint specific to and only reported for MCTD participants

End point values	MHV370 200mg - MCTD	Placebo - MCTD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	0[23]		
Units: liters (L)				
arithmetic mean (standard deviation)	0.250 (± 999)	()		

Notes:

[23] - The insufficient sampling scheme did not allow to provide the data.

Statistical analyses

No statistical analyses for this end point

Secondary: MCTD participants: Diffusing capacity of the lungs for carbon monoxide (DLCO)

End point title	MCTD participants: Diffusing capacity of the lungs for carbon monoxide (DLCO)[24]

End point description:

Diffusing capacity of the lungs for carbon monoxide (DLCO) is a measurement to assess the ability of the lungs to transfer gas from inspired air to the bloodstream. Inhaled carbon monoxide (CO) is used for this test due to its high affinity for hemoglobin. During a ten-second breath-hold, DLCO measures uptake of CO per time per CO pressure. The outcome is presented as percentage of predicted DLCO value. Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'. The Number of Subjects Analyzed differs as stated on the category column, in case of difference from Number of subjects that started the Arm.

End point type	Secondary

End point timeframe:

Baseline, Week 24

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint specific to and only reported for MCTD participants

End point values	MHV370 200mg - MCTD	Placebo - MCTD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	2		
Units: percentage of predicted DLCO				
arithmetic mean (standard deviation)				
Baseline	84.0 (± 999)	95.5 (± 2.12)		
Week 24 (n= 0, 0)	999 (± 999)	999 (± 999)		

Statistical analyses

No statistical analyses for this end point

Secondary: MCTD participants: Change from baseline in King's Brief Interstitial Lung Disease (K-BILD)

End point title	MCTD participants: Change from baseline in King's Brief Interstitial Lung Disease (K-BILD)[25]

End point description:

The K-BILD questionnaire is a self-administered health-status questionnaire that has been developed in patients with interstitial lung diseases. It consists of 15 items in three domains: breathlessness and activities, psychological factors, and chest symptoms. Total scores range from 0 to 100, with higher scores representing better health status. Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'.
The Number of Subjects Analyzed differs as stated on the category column, in case of difference from Number of subjects that started the Arm.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12 and 24

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Endpoint specific to and only reported for MCTD participants

End point values	MHV370 200mg - MCTD	Placebo - MCTD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	1		
Units: Score on scale				
arithmetic mean (standard deviation)				
Week 4	3.00 (± 4.243)	-2.00 (± 999)		
Week 8	13.00 (± 9.899)	0.00 (± 999)		
Week 12 (n= 1,0)	21.00 (± 999)	999 (± 999)		
Week 24 (n= 1,0)	58.00 (± 999)	999 (± 999)		

Statistical analyses

No statistical analyses for this end point

Secondary: MCTD participants: Change from baseline in Raynaud’s Condition Score (RCS)

End point title	MCTD participants: Change from baseline in Raynaud’s Condition Score (RCS)[26]

End point description:

The Raynaud's Condition score (RCS) is participant's rating of difficulty considering number of attacks, duration, amount of pain, numbness, or other symptoms caused in the fingers (including painful sores) due to the Raynaud's phenomenon and impact of Raynaud's alone on use of hands every day. An 11-point Likert scale is used to rate the difficulty caused by the condition with 0 = no difficulty and 10 = extreme difficulty. Participants are asked to select the number that best describes their difficulty, with higher score indicating worse condition. Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating ‘not applicable’). Therefore, not applicable values are indicated as ‘999’.
The Number of Subjects Analyzed differs as stated on the category column, in case of difference from Number of subjects that started the Arm.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 12 and 24

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint specific to and only reported for MCTD participants

End point values	MHV370 200mg - MCTD	Placebo - MCTD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	2		
Units: Score on scale				
arithmetic mean (standard deviation)				
Week 4 (n= 2,1)	-2.50 (± 3.536)	1.00 (± 999)		
Week 12 (n= 1,0)	-1.00 (± 999)	999 (± 999)		
Week 24 (n= 1,0)	-2.00 (± 999)	999 (± 999)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Adverse events were reported from first dose of study treatment until end of study treatment plus 30 days post treatment, up to a maximum duration of approximately 199 days.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups	
Reporting group title	MHV370 200 mg b.i.d
Reporting group description: MHV370 200 mg b.i.d	
Reporting group title	Placebo
Reporting group description: Placebo	
Reporting group title	Total
Reporting group description: Total	

Serious adverse events	MHV370 200 mg b.i.d	Placebo	Total
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	MHV370 200 mg b.i.d	Placebo	Total
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 14 (92.86%)	14 / 16 (87.50%)	27 / 30 (90.00%)
Vascular disorders			

Hypertension			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Vasculitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	1 / 30 (3.33%)
occurrences (all)	2	0	2
General disorders and administration site conditions			
Feeling hot			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	2	2
Malaise			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Pyrexia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Asthenia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Swelling			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Immune system disorders			
Allergy to arthropod bite			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	3 / 14 (21.43%)	2 / 16 (12.50%)	5 / 30 (16.67%)
occurrences (all)	3	2	5
Cough			

subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Productive cough			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Alanine aminotransferase increased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Amylase increased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Antinuclear antibody increased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Blood creatinine increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Complement factor C3 decreased			
subjects affected / exposed	0 / 14 (0.00%)	2 / 16 (12.50%)	2 / 30 (6.67%)
occurrences (all)	0	2	2
Complement factor C4 decreased			

subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Glomerular filtration rate decreased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Neutrophil count decreased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Weight increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Cardiac disorders			
Extrasystoles			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Sinus bradycardia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	1 / 30 (3.33%)
occurrences (all)	2	0	2
Palpitations			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	2	2
Nervous system disorders			
Sciatica			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Neuralgia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Hypergeusia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Headache			
subjects affected / exposed	2 / 14 (14.29%)	6 / 16 (37.50%)	8 / 30 (26.67%)
occurrences (all)	2	8	10
Facial paralysis			

subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Dizziness			
subjects affected / exposed	1 / 14 (7.14%)	1 / 16 (6.25%)	2 / 30 (6.67%)
occurrences (all)	1	3	4
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Leukopenia			
subjects affected / exposed	0 / 14 (0.00%)	3 / 16 (18.75%)	3 / 30 (10.00%)
occurrences (all)	0	3	3
Iron deficiency anaemia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Anaemia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Neutropenia			
subjects affected / exposed	0 / 14 (0.00%)	3 / 16 (18.75%)	3 / 30 (10.00%)
occurrences (all)	0	3	3
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Eye disorders			
Conjunctival suffusion			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Cataract			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Abdominal distension			

subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Parotid gland enlargement			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Paraesthesia oral			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Nausea			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Mouth swelling			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Hiatus hernia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Gastritis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Duodenitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Dry mouth			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Diarrhoea			
subjects affected / exposed	1 / 14 (7.14%)	2 / 16 (12.50%)	3 / 30 (10.00%)
occurrences (all)	2	2	4
Dental caries			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	2	2
Aphthous ulcer			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Abdominal pain upper			

subjects affected / exposed	0 / 14 (0.00%)	2 / 16 (12.50%)	2 / 30 (6.67%)
occurrences (all)	0	2	2
Constipation			
subjects affected / exposed	1 / 14 (7.14%)	1 / 16 (6.25%)	2 / 30 (6.67%)
occurrences (all)	2	1	3
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Cutaneous vasculitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Acne			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Endocrine disorders			
Thyroid mass			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Musculoskeletal and connective tissue disorders			
Vertebral foraminal stenosis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Myalgia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Back pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Arthralgia			
subjects affected / exposed	2 / 14 (14.29%)	1 / 16 (6.25%)	3 / 30 (10.00%)
occurrences (all)	2	1	3
Infections and infestations			
COVID-19			
subjects affected / exposed	4 / 14 (28.57%)	2 / 16 (12.50%)	6 / 30 (20.00%)
occurrences (all)	4	2	6

Cystitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Dacryocanaliculitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Helicobacter infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Herpes zoster			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Nasopharyngitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Otitis media			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Pharyngitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Rash pustular			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Rhinitis			
subjects affected / exposed	2 / 14 (14.29%)	1 / 16 (6.25%)	3 / 30 (10.00%)
occurrences (all)	2	1	3
Upper respiratory tract infection			
subjects affected / exposed	1 / 14 (7.14%)	1 / 16 (6.25%)	2 / 30 (6.67%)
occurrences (all)	1	2	3
Urinary tract infection			
subjects affected / exposed	1 / 14 (7.14%)	1 / 16 (6.25%)	2 / 30 (6.67%)
occurrences (all)	1	1	2
Viral infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	1	1

Metabolism and nutrition disorders			
Dyslipidaemia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	2	2
Hypercholesterolaemia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Hypertriglyceridaemia			
subjects affected / exposed	0 / 14 (0.00%)	2 / 16 (12.50%)	2 / 30 (6.67%)
occurrences (all)	0	3	3
Hyperuricaemia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 16 (6.25%)	2 / 30 (6.67%)
occurrences (all)	1	1	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 August 2021	The reason for this amendment was to update the exclusion criteria and assessment schedule, changed ECG from local to central assessments, SAE reporting, and revised the protocol summary to reflect cardiovascular disease or ECG abnormalities (indicating significant safety risk for the participants) as key exclusion criterion.
29 September 2021	The reason for this amendment was to update the exclusion criteria, laboratory evaluations, discontinuation from study treatment criteria, and the study stopping rules.
09 May 2022	The reason for this amendment was to update the discontinuation criteria for those patients that test positive for SARS-CoV-2 based on emergent data. Also, added a secondary efficacy endpoint called 'STAR', and added an interim analysis planned after approximately 50% of SjS participants had completed 24 (and not 12) weeks of treatment to evaluate the efficacy of MHV370.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported