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Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Not applicable

Trial Indication(s)

Moderate to severe Sjogren's Syndrome or Mixed Connective Tissue Disease

Protocol Number

CMHV370A12201

Protocol Title

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

Clinical Trial Phase

Phase 2

Phase of Drug Development

Phase 2

Study Start/End Dates

Study Start Date: November 30, 2021 (Actual)
Primary Completion Date: February 07, 2023 (Actual)

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Study Completion Date: March 07, 2023 (Actual)

Reason for Termination

Sponsor decision

Study Design/Methodology

This was a phase 2 randomized, participant- and investigator blinded, placebo-controlled, multi-center, parallel group basket study to evaluate the safety, tolerability and efficacy of MHV370 in participants with moderate to severe Sjogren's Syndrome (SjS) or participants with diagnosis of Mixed Connective Tissue Disease (MCTD). Study participants receiving concomitant therapy for their underlying disease who met entry criteria were able to remain on this therapy provided it remained stable until the end of the study.

Approximately 48 participants with SjS and 12 participants with MCTD were planned to be randomized to MHV370 or placebo in a 1:1 ratio. Since the study was terminated early, only 30 participants were enrolled.

Centers

10 centers in 6 countries/regions: Germany(1), Spain(1), Hungary(2), China(2), Taiwan(1), Poland(3)

Objectives:

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.

The secondary objectives of the trial were:

- To evaluate the efficacy of MHV370 compared to placebo based on change from baseline on patient and physician-reported outcomes in SjS and MCTD participants.
- To evaluate the safety and tolerability of MHV370 in SjS and MCTD participants.
- To assess PK parameters of MHV370 in SjS and MCTD participants.
- To explore the effect of MHV370 on quantitative salivary flow (unstimulated) in SjS participants.
- To explore the effect of MHV370 on quantitative tear production in SjS participants.
- To explore the effect of MHV370 on the rate of STAR responders in SjS participants.
- To evaluate the efficacy of MHV370 based on change from baseline in Forced Vital Capacity (FVC) and Forced Expiratory Volume (FEV1, FEV2, FEV3) in MCTD participants.
- To evaluate the efficacy of MHV370 based on change from baseline in the diffusing capacity of lungs for carbon monoxide (DLCO) in MCTD participants.
- To evaluate the efficacy of MHV370 based on change from baseline in the patient reported outcome on lung function in MCTD participants.
- To evaluate the efficacy of MHV370 based on change from baseline in Raynaud's Condition Score (RCS) in MCTD participants.

Test Product (s), Dose(s), and Mode(s) of Administration

Participants received oral dose twice daily of MHV370 200 mg or matching placebo. Participants took 2 hard gelatin capsules of 100 mg at each dose to make up to 200 mg.

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Statistical Methods

Analysis sets:

• The Safety analysis set included all participants who received any study drug.

• The PK analysis set included all participants with at least one available valid (i.e., not flagged for exclusion) PK concentration measurement, who received the investigational study drug (MHV370) and with no protocol deviations with impact on PK data.

• The PD analysis set included all participants who received any study drug and had no protocol deviations with relevant impact on PD/efficacy data.

Analysis of the primary endpoint

For SjS: The primary endpoint is the change from baseline in ESSDAI total score at Week 24, defined as the Week 24 visit ESSDAI total score minus the baseline ESSDAI total score. A negative change indicates an improvement of disease activity.

Descriptive statistics (raw and change from baseline) were provided by treatment group and visit/time.

For MCTD: The primary endpoint is the change from baseline in PhGA (ranging from “no disease activity” (0) to “maximal disease activity” (100) after 24 weeks of treatment. It is defined as the Week 24 visit PhGA value minus the baseline PhGA value. A negative change indicates an improvement in disease activity. Descriptive statistics (raw and change from baseline) were provided by treatment group and visit/time.

Analysis of secondary endpoints

All analyses of secondary efficacy endpoints were performed on the PD analysis set.

SjS: For the analysis of the secondary endpoints ESSPRI, FACIT-F, PhGA, Schirmer’s test and salivary flow rate, descriptive summary statistics (raw and change from baseline) were provided by endpoint, treatment group and visit/time.

For the secondary endpoint STAR, responder status in STAR was assessed at Weeks 4, 12 and 24. Descriptive frequency data were provided by treatment group and visit/time. Missing responses were treated as non-responders. The percentage of responders together with the 95% confidence interval (Clopper-Pearson method) was presented along with p-values from Fisher’s exact test for the difference between treatment groups.

MCTD: For the secondary endpoints FVC, FEV1, FEV2, FEV3, RCS, FACIT F, DLCO, K-BILD, PhGA and ESSDAI (articular and pulmonary domains only) descriptive summary statistics (raw and change from baseline) were provided by endpoint, treatment group and visit/time. Graphical methods, such as arithmetic mean or spaghetti plots were employed for each endpoint.

PK analysis:

PK analysis set was used for the PK analyses.

Descriptive summary statistics for PK concentration data were provided by treatment group and nominal sampling time point, including the frequency (n, %) of concentrations below the lower limit of quantification (LLOQ) which were reported as zero.

Analysis of safety

Safety analysis set was used for the safety analyses.

All safety endpoints were listed and summarized by treatment group for all participants in the safety analysis set.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:

SjS and MCTD:
• Fully vaccinated with any locally approved COVID-19 vaccination including booster vaccinations if required by local guidelines

SjS:
• Unstimulated whole salivary flow rate of > 0 mL/min at screening
• Classification of Sjögren's Syndrome according to the 2016 ACR/EULAR criteria at screening
• Screening ESSDAI (based on weighted score) ≥ 5 from 8 defined domains (biologic, hematologic, articular, cutaneous, glandular, lymphadenopathy, renal, constitutional).

MCTD:
• Diagnosis of MCTD based on criteria like a) Raynaud’s phenomenon b) At least two of the four following signs: i) synovitis, ii) myositis, iii) swollen fingers and vi) interstitial lung disease
• Patients with overlap syndromes, i.e. patients meeting diagnostic criteria for systemic autoimmune disease other than MCTD may be included unless they have major organ involvement as judged by the investigator

Exclusion Criteria:

SjS and MCTD:
• Prior use of B-cell depleting therapy within 6 months of baseline. For participants who received B-cell depleting therapy within 6 -12 months of baseline visit, B-cell count should be within normal range
• Prior treatment with any of the following within 3 months of baseline: CTLA4-Fc Ig (abatacept), Anti-TNF mAb, Intravenous Ig, Plasmapheresis, i.v. or oral cyclophosphamide, i.v. or oral cyclosporine A
• Screening CBC laboratory values as follows: Hemoglobin levels < 8 g/dL (< 5 mmol/L), Total leukocyte count < 2,000/µL (2 x 109/L), Platelets < 50,000/µL (50 x 109/L), Neutrophil count < 1,000/µL (1 x 109/L)
• Pregnant or nursing (lactating) women
• Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant, unless they use a highly effective method of contraception

SjS:
• Sjögren's Syndrome overlap syndromes where another autoimmune disease constitutes the primary illness
• Required regular use of medications known to cause, as a major side effect, dry mouth / eyes

Other protocol-defined inclusion/exclusion criteria may apply

Participant Flow Table

Overall Study

	MHV370 200mg - SjS	Placebo - SjS	MHV370 200mg - MCTD	Placebo - MCTD	Total
Arm/Group Description	MHV370 200mg oral dose, twice daily. SjS participants.	Placebo oral dose, twice daily. SjS participants.	MHV370 200mg oral dose, twice daily. MCTD participants.	Placebo oral dose, twice daily. MCTD participants.	
Started	12	14	2	2	30
Completed	0	4	1	0	5
Not Completed	12	10	1	2	25
Adverse Event	4	0	0	0	4

Withdrawal by Subject	1	1	0	0	2
Technical problems	7	9	1	2	19

Baseline Characteristics

	MHV370 200mg - SjS	Placebo - SjS	MHV370 200mg - MCTD	Placebo - MCTD	Total
Arm/Group Description	MHV370 200mg oral dose, twice daily. SjS participants.	Placebo oral dose, twice daily. SjS participants.	MHV370 200mg oral dose, twice daily. MCTD participants.	Placebo oral dose, twice daily. MCTD participants.	
Number of Participants [units: participants]	12	14	2	2	30
Baseline Analysis Population Description					
Age Continuous (units: years) Analysis Population Type: Participants Mean ± Standard Deviation					
	49.3±12.20	54.7±9.67	35.0±12.73	44.0±0.00	50.5±11.52
Sex: Female, Male (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)					
Female	12	14	2	2	30
Male	0	0	0	0	0
Race/Ethnicity, Customized (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)					
Asian	3	3	0	0	6

White	9	11	2	2	24

Primary Outcome Result(s)

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

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.
Time Frame	Baseline, Week 24
Analysis Population Description	The pharmacodynamic (PD) analysis set included all participants who received any study drug and had no protocol deviations with relevant impact on PD/efficacy data. The data includes only participants who completed Week 24. Only participants with evaluable records are included.

	MHV370 200mg - SjS	**Placebo - SjS**
Arm/Group Description	MHV370 200mg oral dose, twice daily. SjS participants.	Placebo oral dose, twice daily. SjS participants.
Number of Participants Analyzed [units: participants]	0	4
SjS participants: Change from baseline in Eular Sjögren's Disease Activity Index (ESSDAI) after 24 weeks of treatment (units: Score on scale)	**Mean ± Standard Error**	**Mean ± Standard Error**
		-4.39 ± 2.41

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

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.
Time Frame	Baseline, Week 24
Analysis Population Description	The pharmacodynamic (PD) analysis set included all participants who received any study drug and had no protocol deviations with relevant impact on PD/efficacy data. The data includes only participants who completed Week 24. Only participants with evaluable records are included.

	MHV370 200mg - MCTD	Placebo - MCTD
Arm/Group Description	MHV370 200mg oral dose, twice daily. MCTD participants.	Placebo oral dose, twice daily. MCTD participants.
Number of Participants Analyzed [units: participants]	1	0
MCTD participants: Change from baseline in physician's global assessment scale (PhGA) after 24 weeks of treatment (units: Score on scale)	**Median (Full Range)**	**Median (Full Range)**
	-62.00 (-62.00 to -62.00)	

Secondary Outcome Result(s)

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

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

Analysis Population Description	The pharmacokinetic (PK) analysis set included participants with at least one available valid (i.e., not flagged for exclusion) PK concentration measurement, who received MHV370 and with no protocol deviations with impact on PK data. Only participants with evaluable records are included.

	MHV370 200mg - SjS	MHV370 200mg - MCTD
Arm/Group Description	MHV370 200mg oral dose, twice daily. SjS participants.	MHV370 200mg oral dose, twice daily. MCTD participants
Number of Participants Analyzed [units: participants]	8	1
SjS and MCTD participants: Maximum observed plasma concentrations (Cmax) of MHV370 at steady state (units: ng/mL)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
	278 ± 85.7	194

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

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.
Time Frame	pre-dose, 0.5, 1, 2 ,4 and 6 hours after dosing at week 4
Analysis Population Description	The pharmacokinetic (PK) analysis set included participants with at least one available valid (i.e., not flagged for exclusion) PK concentration measurement, who received MHV370 and with no protocol deviations with impact on PK data. Only participants with evaluable records are included.

	MHV370 200mg - SjS	MHV370 200mg - MCTD
Arm/Group Description	MHV370 200mg oral dose, twice daily. SjS participants.	MHV370 200mg oral dose, twice daily. MCTD participants.
Number of Participants Analyzed [units: participants]	5	1

SjS and MCTD participants: Area under the plasma concentration-time curve from time zero to 6 hours (AUC0-6h) of MHV370 (units: ng*h/mL)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
	1060 ± 462	742

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

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.
Time Frame	pre-dose, 0.5, 1, 2 ,4 and 6 hours after dosing at week 4
Analysis Population Description	The pharmacokinetic (PK) analysis set included participants with at least one available valid (i.e., not flagged for exclusion) PK concentration measurement, who received MHV370 and with no protocol deviations with impact on PK data. Only participants with evaluable records are included.

	MHV370 200mg - SjS	**MHV370 200mg - MCTD**
Arm/Group Description	MHV370 200mg oral dose, twice daily. SjS participants.	MHV370 200mg oral dose, twice daily. - MCTD participants
Number of Participants Analyzed [units: participants]	8	1
SjS and MCTD participants: Time to reach maximum plasma concentrations (Tmax) of MHV370 at steady state (units: hours)	**Median (Full Range)**	**Median (Full Range)**
Week 4	1.50 (1.00 to 4.00)	2.00

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

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.

Time Frame: Baseline, Weeks 4, 8, 12, 20 and 24

Analysis Population Description: The pharmacodynamic (PD) analysis set included all participants who received any study drug and had no protocol deviations with relevant impact on PD/efficacy data. Data from participants who have discontinued treatment early are regarded as missing after the treatment discontinuation. Only participants with evaluable records are included.

	MHV370 200mg - SjS	Placebo - SjS	MHV370 200mg - MCTD	Placebo - MCTD
Arm/Group Description	MHV370 200mg oral dose, twice daily. SjS participants.	Placebo oral dose, twice daily. SjS participants.	MHV370 200mg oral dose, twice daily. MCTD participants.	Placebo oral dose, twice daily. MCTD participants.
Number of Participants Analyzed [units: participants]	8	12	2	1
SjS and MCTD participants: Change from baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) scale (units: Score on scale)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
Week 4	0.13 ± 3.271	-1.58 ± 6.052	15.50 ± 9.192	-3.00
Week 8 (n= 7,10,2,1)	3.14 ± 5.928	-2.80 ± 4.185	20.00 ± 7.071	-2.00
Week 12 (n= 4,7,1,0)	-1.25 ± 6.702	2.71 ± 8.826	20.00	
Week 20 (n= 1,5,1,0)	-9.42	4.80 ± 8.758	23.00	
Week 24 (n= 0,4,1,0)		5.75 ± 10.782	30.00	

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

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.

Time Frame: Baseline, Weeks 4, 8, 12, 20 and 24

Analysis Population Description	The pharmacodynamic (PD) analysis set included all participants who received any study drug and had no protocol deviations with relevant impact on PD/efficacy data. Data from participants who have discontinued treatment early are regarded as missing after the treatment discontinuation. Only participants with evaluable records are included.

	MHV370 200mg - SjS	Placebo - SjS	MHV370 200mg - MCTD	Placebo - MCTD
Arm/Group Description	MHV370 200mg oral dose, twice daily. SjS participants.	Placebo oral dose, twice daily. SjS participants.	MHV370 200mg oral dose, twice daily. MCTD participants.	Placebo oral dose, twice daily. MCTD participants.
Number of Participants Analyzed [units: participants]	8	12	2	1
SjS and MCTD participants: Change from baseline in Physician Global Assessment (PhGA) (units: Score on scale)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
Week 4	-1.75 ± 12.658	-5.25 ± 11.185	-20.50 ± 12.021	-15.00
Week 8 (n= 7,10,2,1)	2.57 ± 12.608	-8.90 ± 11.474	-39.00 ± 18.385	-12.50
Week 12 (n= 4,7,1,0)	-4.00 ± 20.559	-19.43 ± 14.328	-66.00	
Week 20 (n= 1,5,1,0)	3.00	-14.60 ± 22.423	-64.00	
Week 24 (n= 0,4,1,0)		-30.75 ± 19.534	-62.00	

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

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.
Time Frame	Baseline, Weeks 4, 8, 12, 20 and 24
Analysis Population Description	The pharmacodynamic (PD) analysis set included all participants who received any study drug and had no protocol deviations with relevant impact on PD/efficacy data. Only participants with evaluable records are included.

	MHV370 200mg - SjS	Placebo - SjS
Arm/Group Description	MHV370 200mg oral dose, twice daily. SjS participants.	Placebo oral dose, twice daily. SjS participants.
Number of Participants Analyzed [units: participants]	8	12
SjS participants: Change from baseline in Eular Sjögren's Syndrome Disease Activity Index (ESSDAI) (units: Score on scale)	**Mean ± Standard Deviation**	**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	0.00 ± 14.629
Week 24 (n= 0,4)		-0.25 ± 11.117

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

Description	The ESSPRI is an established 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 ESSPRI score is calculated as the mean of the three individual domains where all domains carry the same weight. Minimum score can be 0 and maximum score can be 10, where a higher ESSPRI score indicates more severe symptoms. A negative change score from baseline indicates improvement.
Time Frame	baseline, weeks 4, 8, 12, 20 and 24
Analysis Population Description	The pharmacodynamic (PD) analysis set included all participants who received any study drug and had no protocol deviations with relevant impact on PD/efficacy data. Only participants with evaluable records are included.

	MHV370 200mg - SjS	Placebo - SjS
Arm/Group Description	MHV370 200mg oral dose, twice daily. SjS participants.	Placebo oral dose, twice daily. SjS participants.

Number of Participants Analyzed [units: participants]	8	12
SjS participants: Change from baseline in Eular Sjögren's Syndrome Patient Reported Index (ESSPRI) (units: Score on scale)	**Mean ± Standard Deviation**	**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	-2.20 ± 1.865
Week 24 (n= 0,4)		-2.00 ± 2.000

SjS participants: Change from baseline to the salivary flow rate

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.
Time Frame	Baseline, Weeks 4, 12 and 24
Analysis Population Description	The pharmacodynamic (PD) analysis set included all participants who received any study drug and had no protocol deviations with relevant impact on PD/efficacy data.

	MHV370 200mg - SjS	**Placebo - SjS**
Arm/Group Description	MHV370 200mg oral dose, twice daily. SjS participants.	Placebo oral dose, twice daily. SjS participants.
Number of Participants Analyzed [units: participants]	12	14
SjS participants: Change from baseline to the salivary flow rate (units: mL/min)	**Mean ± Standard Deviation**	**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)	0.564 ± 0.9193

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

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.
Time Frame	Baseline, Week 4, 12 and 24
Analysis Population Description	The pharmacodynamic (PD) analysis set included all participants who received any study drug and had no protocol deviations with relevant impact on PD/efficacy data. Only participants with evaluable records are included.

	MHV370 200mg - SjS	**Placebo - SjS**
Arm/Group Description	MHV370 200mg oral dose, twice daily. SjS participants.	Placebo oral dose, twice daily. SjS participants.
Number of Participants Analyzed [units: participants]	12	14
SjS participants: Change from baseline to the Schirmer's test (units: milimeter)	**Mean ± Standard Deviation**	**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)		-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)		-1.0 ± 2.94

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

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.
Time Frame	Baseline, Week 4, 12 and 24
Analysis Population Description	The pharmacodynamic (PD) analysis set included all participants who received any study drug and had no protocol deviations with relevant impact on PD/efficacy data. Missing responses will be treated as non-responders. Only participants with evaluable records are included.

	MHV370 200mg - SjS	**Placebo - SjS**
Arm/Group Description	MHV370 200mg oral dose, twice daily. SjS participants.	Placebo oral dose, twice daily. SjS participants.
Number of Participants Analyzed [units: participants]	12	14
SjS participants: Sjögren's Tool for Assessing Response (STAR) response over time up to week 24 (units: participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Week 4	0 (%)	3 (21.43%)
Week 12	1 (8.33%)	4 (28.57%)
Week 24	0 (%)	2 (14.29%)

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

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.
Time Frame	Baseline, Weeks 4, 8, 12 and 24
Analysis Population Description	The pharmacodynamic (PD) analysis set included all participants who received any study drug and had no protocol deviations with relevant impact on PD/efficacy data. Data from participants who have discontinued treatment early are regarded as missing after the treatment discontinuation. Only participants with evaluable records are included.

	MHV370 200mg - MCTD	**Placebo - MCTD**
Arm/Group Description	MHV370 200mg oral dose, twice daily. MCTD participants.	Placebo oral dose, twice daily. MCTD participants.
Number of Participants Analyzed [units: participants]	2	1
MCTD: Change from baseline in articular and pulmonary domains of the Eular Sjögren's Syndrome Disease Activity Index (ESSDAI) (units: Score on scale)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
Week 4 - articular	0.00 ± 0.000	0.00
Week 8 - articular	-1.00 ± 0.000	0.00
Week 12 – articular (n= 1,0)	-1.00	
Week 24 – articular (n= 1,0)	-2.00	
Week 4 – pulmonary	0.00 ± 0.000	0.00
Week 8 – pulmonary	-0.50 ± 0.707	0.00
Week 12 – pulmonary (n= 1,0)	-1.00	
Week 24 – pulmonary (n= 1,0)	-1.00	

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

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.
Time Frame	Baseline, Week 12
Analysis Population Description	The pharmacodynamic (PD) analysis set included all participants who received any study drug and had no protocol deviations with relevant impact on PD/efficacy data. Data from participants who have discontinued treatment early are regarded as missing after the treatment discontinuation. Only participants with evaluable records are included.

	MHV370 200mg - MCTD	**Placebo - MCTD**
Arm/Group Description	MHV370 200mg oral dose, twice daily. MCTD participants.	Placebo oral dose, twice daily. MCTD participants.
Number of Participants Analyzed [units: participants]	1	0
MCTD participants: Change from baseline in Forced Vital Capacity (FVC) (units: liters (L))	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
Week 12	0.530	

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

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.
Time Frame	Baseline, Week 12
Analysis Population Description	The pharmacodynamic (PD) analysis set included all participants who received any study drug and had no protocol deviations with relevant impact on PD/efficacy data. Data from participants who have discontinued treatment early are regarded as missing after the treatment discontinuation. Only participants with evaluable records are included.

	MHV370 200mg - MCTD	**Placebo - MCTD**

Arm/Group Description	MHV370 200mg oral dose, twice daily. MCTD participants.	Placebo oral dose, twice daily. MCTD participants.
Number of Participants Analyzed [units: participants]	1	0
MCTD participants: Change from baseline in Forced expiratory volume during the first second (FEV1) of a forced breath (units: liters (L))	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
Week 12	0.250	

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

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.
Time Frame	Baseline, Week 12
Analysis Population Description	The pharmacodynamic (PD) analysis set included all participants who received any study drug and had no protocol deviations with relevant impact on PD/efficacy data. Data from participants who have discontinued treatment early are regarded as missing after the treatment discontinuation. Only participants with evaluable records are included.

	MHV370 200mg - MCTD	**Placebo - MCTD**
Arm/Group Description	MHV370 200mg oral dose, twice daily. MCTD participants.	Placebo oral dose, twice daily. MCTD participants.
Number of Participants Analyzed [units: participants]	1	0
MCTD participants: Change from baseline in Forced expiratory volume during the first two seconds (FEV2) of a forced breath (units: liters (L))	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
Week 12	0.410	

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

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.
Time Frame	Baseline, Week 12
Analysis Population Description	The pharmacodynamic (PD) analysis set included all participants who received any study drug and had no protocol deviations with relevant impact on PD/efficacy data. Data from participants who have discontinued treatment early are regarded as missing after the treatment discontinuation. Only participants with evaluable records are included.

	MHV370 200mg - MCTD	**Placebo - MCTD**
Arm/Group Description	MHV370 200mg oral dose, twice daily. MCTD participants.	Placebo oral dose, twice daily. MCTD participants.
Number of Participants Analyzed [units: participants]	1	0
MCTD participants: Change from baseline in Forced expiratory volume during the first three seconds (FEV3) of a forced breath (units: liters (L))	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
Week 12	0.460	

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

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.
Time Frame	Baseline, Week 24
Analysis Population Description	The pharmacodynamic (PD) analysis set included all participants who received any study drug and had no protocol deviations with relevant impact on PD/efficacy data. Data from participants who have discontinued treatment early are regarded as missing after the treatment discontinuation. Only participants with evaluable records are included.

	MHV370 200mg - MCTD	**Placebo - MCTD**

Arm/Group Description	MHV370 200mg oral dose, twice daily. MCTD participants.	Placebo oral dose, twice daily. MCTD participants.
Number of Participants Analyzed [units: participants]	1	2
MCTD participants: Diffusing capacity of the lungs for carbon monoxide (DLCO) (units: percentage of predicted DLCO)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
Baseline	84.0	95.5 ± 2.12
Week 24 (n=0,0)		

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

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.
Time Frame	Baseline, Weeks 4, 8, 12 and 24
Analysis Population Description	The pharmacodynamic (PD) analysis set included all participants who received any study drug and had no protocol deviations with relevant impact on PD/efficacy data. Data from participants who have discontinued treatment early are regarded as missing after the treatment discontinuation. Only participants with evaluable records are included.

	MHV370 200mg - MCTD	**Placebo - MCTD**
Arm/Group Description	MHV370 200mg oral dose, twice daily. MCTD participants.	Placebo oral dose, twice daily. MCTD participants.
Number of Participants Analyzed [units: participants]	2	1
MCTD participants: Change from baseline in King's Brief Interstitial Lung Disease (K-BILD) (units: Score on scale)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
Week 4	3.00 ± 4.243	-2.00
Week 8	13.00 ± 9.899	0.00
Week 12 (n= 1,0)	21.00	

Week 24 (n= 1,0)	58.00

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

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.
Time Frame	Baseline, Weeks 4, 12 and 24
Analysis Population Description	The pharmacodynamic (PD) analysis set included all participants who received any study drug and had no protocol deviations with relevant impact on PD/efficacy data. Data from participants who have discontinued treatment early are regarded as missing after the treatment discontinuation. Only participants with evaluable records are included.

	MHV370 200mg - MCTD	**Placebo - MCTD**
Arm/Group Description	MHV370 200mg oral dose, twice daily. MCTD participants.	Placebo oral dose, twice daily. MCTD participants.
Number of Participants Analyzed [units: participants]	2	2
MCTD participants: Change from baseline in Raynaud's Condition Score (RCS) (units: Score on scale)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
Week 4 (n= 2,1)	-2.50 ± 3.536	1.00
Week 12 (n= 1,0)	-1.00	
Week 24 (n= 1,0)	-2.00	

Safety Results

Time Frame	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.
Source Vocabulary for Table Default	MedDRA (25.1)
Collection Approach for Table Default	Systematic Assessment

All-Cause Mortality

	sjs_MHV N = 12	**sjs_Placebo N = 14**	**MCTD_MHV N = 2**	**MCTD_Placebo N = 2**	**Total N = 30**
Arm/Group Description	sjs_MHV	sjs_Placebo	MCTD_MHV	MCTD_Placebo	Total
Total Number Affected	0	0	0	0	0
Total Number At Risk	12	14	2	2	30

Serious Adverse Events

	sjs_MHV N = 12	**sjs_Placebo N = 14**	**MCTD_MHV N = 2**	**MCTD_Placebo N = 2**	**Total N = 30**
Arm/Group Description	sjs_MHV	sjs_Placebo	MCTD_MHV	MCTD_Placebo	Total
Total # Affected by any Serious Adverse Event	0	0	0	1	1
Total # at Risk by any Serious Adverse Event	12	14	2	2	30
Reproductive system and breast disorders					

Ovarian cyst	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00%)	1 (3.33%)

Other (Not Including Serious) Adverse Events

Frequent Event Reporting Threshold 5%

	sjs_MHV N = 12	sjs_Placebo N = 14	MCTD_MHV N = 2	MCTD_Placebo N = 2	Total N = 30
Arm/Group Description	sjs_MHV	sjs_Placebo	MCTD_MHV	MCTD_Placebo	Total
Total # Affected by any Other Adverse Event	12	12	1	2	27
Total # at Risk by any Other Adverse Event	12	14	2	2	30
Blood and lymphatic system disorders					
Anaemia	0 (0.00%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Iron deficiency anaemia	0 (0.00%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Leukopenia	0 (0.00%)	3 (21.43%)	0 (0.00%)	0 (0.00%)	3 (10.00%)
Lymphopenia	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Neutropenia	0 (0.00%)	3 (21.43%)	0 (0.00%)	0 (0.00%)	3 (10.00%)
Cardiac disorders					
Extrasystoles	0 (0.00%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Palpitations	0 (0.00%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Sinus bradycardia	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)

Ear and labyrinth disorders					
Tinnitus	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Endocrine disorders					
Thyroid mass	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Eye disorders					
Cataract	0 (0.00%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Conjunctival suffusion	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Gastrointestinal disorders					
Abdominal distension	0 (0.00%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Abdominal pain	0 (0.00%)	0 (0.00%)	1 (50.00%)	0 (0.00%)	1 (3.33%)
Abdominal pain upper	0 (0.00%)	2 (14.29%)	0 (0.00%)	0 (0.00%)	2 (6.67%)
Aphthous ulcer	0 (0.00%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Constipation	1 (8.33%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	2 (6.67%)
Dental caries	0 (0.00%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Diarrhoea	1 (8.33%)	1 (7.14%)	0 (0.00%)	1 (50.00%)	3 (10.00%)
Dry mouth	0 (0.00%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Duodenitis	0 (0.00%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Gastritis	0 (0.00%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Hiatus hernia	0 (0.00%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Mouth swelling	0 (0.00%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Nausea	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00%)	1 (3.33%)
Paraesthesia oral	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00%)	1 (3.33%)
Parotid gland enlargement	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)

General disorders and administration site conditions					
Asthenia	0 (0.00%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Feeling hot	0 (0.00%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Malaise	0 (0.00%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Pyrexia	0 (0.00%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Swelling	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Immune system disorders					
Allergy to arthropod bite	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Infections and infestations					
COVID-19	4 (33.33%)	2 (14.29%)	0 (0.00%)	0 (0.00%)	6 (20.00%)
Cystitis	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Dacryocanaliculitis	0 (0.00%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Helicobacter infection	0 (0.00%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Herpes zoster	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Nasopharyngitis	0 (0.00%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Otitis media	0 (0.00%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Pharyngitis	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Rash pustular	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Rhinitis	2 (16.67%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	3 (10.00%)
Upper respiratory tract infection	1 (8.33%)	0 (0.00%)	0 (0.00%)	1 (50.00%)	2 (6.67%)
Urinary tract infection	1 (8.33%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	2 (6.67%)
Viral infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00%)	1 (3.33%)
Investigations					

Activated partial thromboplastin time prolonged	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Alanine aminotransferase increased	0 (0.00%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Amylase increased	0 (0.00%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Antinuclear antibody increased	0 (0.00%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Aspartate aminotransferase increased	0 (0.00%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Blood creatine phosphokinase increased	0 (0.00%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Blood creatinine increased	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Complement factor C3 decreased	0 (0.00%)	2 (14.29%)	0 (0.00%)	0 (0.00%)	2 (6.67%)
Complement factor C4 decreased	0 (0.00%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Glomerular filtration rate decreased	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Neutrophil count decreased	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Weight increased	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Metabolism and nutrition disorders					
Dyslipidaemia	0 (0.00%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Hypercholesterolaemia	0 (0.00%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Hypertriglyceridaemia	0 (0.00%)	2 (14.29%)	0 (0.00%)	0 (0.00%)	2 (6.67%)
Hyperuricaemia	1 (8.33%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	2 (6.67%)
Musculoskeletal and connective tissue disorders					
Arthralgia	2 (16.67%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	3 (10.00%)
Back pain	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Myalgia	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Vertebral foraminal stenosis	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)

Nervous system disorders					
Dizziness	1 (8.33%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	2 (6.67%)
Facial paralysis	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Headache	2 (16.67%)	4 (28.57%)	0 (0.00%)	2 (100.00%)	8 (26.67%)
Hypergeusia	0 (0.00%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Neuralgia	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Sciatica	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Psychiatric disorders					
Insomnia	0 (0.00%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Reproductive system and breast disorders					
Ovarian cyst	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00%)	1 (3.33%)
Respiratory, thoracic and mediastinal disorders					
Cough	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Oropharyngeal pain	3 (25.00%)	2 (14.29%)	0 (0.00%)	0 (0.00%)	5 (16.67%)
Productive cough	0 (0.00%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Skin and subcutaneous tissue disorders					
Acne	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Cutaneous vasculitis	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Dermatitis allergic	0 (0.00%)	0 (0.00%)	1 (50.00%)	0 (0.00%)	1 (3.33%)
Vascular disorders					
Hypertension	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)
Vasculitis	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)

Conclusion:

Overall, MHV370 was generally safe and well tolerated in adults with Sjogren´s Syndrome (SjS) and Mixed Connective Tissue Disease (MCTD). Due to the early termination of the study, leading to the inclusion of only 30 participants (26 with SjS and 4 with MCTD), and the majority of participants having their treatment discontinued prematurely, the efficacy results cannot be adequately interpreted. The plasma exposure of MHV370 after multiple oral dosing was in a range that was comparable to the first-in-man trial. The most commonly observed adverse events (AEs) were headache and oropharyngeal pain, and the majority of the AEs were mild in intensity. There were no deaths reported and 1 serious adverse event reported in the MCTD placebo group.

Date of Clinical Trial Report

9-October-2023