Clinical trial results:
Study of safety and efficacy of multiple VAY736 doses in patients with moderate to severe primary Sjogren's Syndrome (pSS)

Summary

EudraCT number	2016-003292-22
Trial protocol	DE ES PT GB FR NL HU BE AT PL IT RO
Global end of trial date	23 September 2021

Results information

Result version number	v1 (current)
This version publication date	11 October 2022
First version publication date	11 October 2022

Trial information

Trial identification

Sponsor protocol code	CVAY736A2201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02962895
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.com
Scientific contact	Study Director, Novartis Pharmaceuticals, 1 862 7788300, 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	23 September 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 June 2020
Global end of trial reached?	Yes
Global end of trial date	23 September 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate a dose response of VAY736 defined as change in ESSDAI from baseline at 24 weeks

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	27 June 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 10
Country: Number of subjects enrolled	Austria: 10
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	Chile: 9
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	Germany: 29
Country: Number of subjects enrolled	United Kingdom: 9
Country: Number of subjects enrolled	Hungary: 8
Country: Number of subjects enrolled	Israel: 3
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	Japan: 12
Country: Number of subjects enrolled	Netherlands: 3
Country: Number of subjects enrolled	Poland: 10
Country: Number of subjects enrolled	Portugal: 9
Country: Number of subjects enrolled	Romania: 4
Country: Number of subjects enrolled	Russian Federation: 15
Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	Taiwan: 7
Country: Number of subjects enrolled	United States: 31

Worldwide total number of subjects	190
EEA total number of subjects	94

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)	163
From 65 to 84 years	27
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

190 Patients were enrolled from 56 centers in 19 countries.

Pre-assignment

Screening details:

Period one was the screening period and is not shown here.

Period 1

Period 1 title	Period 2 - Randomized Set
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Subject, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	No
Arm title	Placebo

Arm description:

Placebo control

Arm type	Placebo
Investigational medicinal product name	PLACEBO
Investigational medicinal product code	PLACEBO
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

S.C.

Arm title	VAY736 5 mg

Arm description:

VAY736 low

Arm type	Experimental
Investigational medicinal product name	VAY736
Investigational medicinal product code	
Other name	ianalumab
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

5 mg s.c.

Arm title	VAY736 50 mg

Arm description:

VAY736 medium

Arm type	Experimental
Investigational medicinal product name	VAY736
Investigational medicinal product code	
Other name	ianalumab
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:
50 mg s.c.

Arm title	VAY736 300 mg
Arm description: VAY736 high	
Arm type	Experimental
Investigational medicinal product name	VAY736
Investigational medicinal product code	
Other name	ianalumab
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:
300 mg s.c.

Number of subjects in period 1	Placebo	VAY736 5 mg	VAY736 50 mg
Started	49	47	47
Completed	47	42	43
Not completed	2	5	4
Consent withdrawn by subject	1	1	2
New therapy for indication	1	-	-
Adverse event, non-fatal	-	2	2
Non-compliance with treatment	-	1	-
Pregnancy	-	-	-
Withdrawal of Informed Consent	-	1	-

Number of subjects in period 1	VAY736 300 mg
Started	47
Completed	46
Not completed	1
Consent withdrawn by subject	-
New therapy for indication	-
Adverse event, non-fatal	-
Non-compliance with treatment	-
Pregnancy	1
Withdrawal of Informed Consent	-

Period 2

Period 2 title	Period 3 - Randomized Set
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	No
Arm title	VAY736 150 mg

Arm description:

Placebo in Period 2 and VAY736 150 mg in Period 3

Arm type	Experimental
Investigational medicinal product name	VAY736
Investigational medicinal product code	
Other name	ianalumab
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

150 mg s.c.

Arm title	VAY736 - Placebo 300 mg

Arm description:

VAY736 300 mg in Period 2 and Placebo in Period 3

Arm type	Experimental
Investigational medicinal product name	VAY736 300 mg - VAY736 300 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Injection

Dosage and administration details:

VAY736 300 mg - VAY736 300 mg

Arm title	VAY736 300 mg - VAY736 300 mg

Arm description:

VAY736 300 mg in Period 2 and Period 3

Arm type	Experimental
Investigational medicinal product name	VAY736
Investigational medicinal product code	
Other name	300 mg vs 300 mg
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Any VAY736

Number of subjects in period 2	VAY736 150 mg	VAY736 - Placebo 300 mg	VAY736 300 mg - VAY736 300 mg
Started	47	22	21
Completed	42	22	17
Not completed	5	0	4
Adverse event, non-fatal	5	-	2
Pregnancy	-	-	1
Patient/guardian decision	-	-	1

Period 3	
Period 3 title	Period 4
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Arms	
Are arms mutually exclusive?	No
Arm title	Placebo
Arm description: Placebo control	
Arm type	Placebo
Investigational medicinal product name	PLACEBO
Investigational medicinal product code	
Other name	PLACEBO
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details: s.c.	
Arm title	VAY736 5 mg
Arm description: VAY736 low	
Arm type	Experimental
Investigational medicinal product name	VAY736
Investigational medicinal product code	
Other name	ianalumab
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details: 5 mg s.c.	
Arm title	VAY736 50 mg
Arm description: VAY736 medium	
Arm type	Experimental

Investigational medicinal product name	VAY736
Investigational medicinal product code	
Other name	ianalumab
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:
50 mg s.c.

Arm title	VAY736 150 mg

Arm description:
Placebo in Period 2 and VAY736 150 mg in Period 3

Arm type	Experimental
Investigational medicinal product name	VAY736
Investigational medicinal product code	
Other name	ianalumab
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:
150 mg s.c.

Arm title	VAY736 300 mg

Arm description:
VAY736 high

Arm type	Experimental
Investigational medicinal product name	VAY736
Investigational medicinal product code	
Other name	ianalumab
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:
300 mg s.c.

Arm title	VAY736 - Placebo 300 mg

Arm description:
VAY736 300 mg in Period 2 and Placebo in Period 3

Arm type	Experimental
Investigational medicinal product name	VAY736 300 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Injection

Dosage and administration details:
VAY736 300 mg

Arm title	VAY736 300 mg - VAY736 300 mg

Arm description:
VAY736 300 mg in Period 2 and Period 3

Arm type	Experimental
Investigational medicinal product name	VAY736 300 mg - VAY736 300 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Injection

Dosage and administration details: VAY736 300 mg - VAY736 300 mg	
Investigational medicinal product name	VAY736 300 mg - VAY736 300 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Injection

Dosage and administration details:
VAY736 300 mg - VAY736 300 mg

Number of subjects in period 3	Placebo	VAY736 5 mg	VAY736 50 mg
Started	2	47	47
Completed	2	41	43
Not completed	0	6	4
Consent withdrawn by subject	-	2	3
New therapy for indication	-	-	-
Lost to follow-up	-	-	-
Withdrawal of Informed Consent	-	3	1
Lack of efficacy	-	1	-

Number of subjects in period 3	VAY736 150 mg	VAY736 300 mg	VAY736 - Placebo 300 mg
Started	46	4	22
Completed	42	1	20
Not completed	4	3	2
Consent withdrawn by subject	2	1	2
New therapy for indication	1	-	-
Lost to follow-up	1	-	-
Withdrawal of Informed Consent	-	2	-
Lack of efficacy	-	-	-

Number of subjects in period 3	VAY736 300 mg - VAY736 300 mg
Started	20
Completed	20
Not completed	0
Consent withdrawn by subject	-
New therapy for indication	-
Lost to follow-up	-
Withdrawal of Informed Consent	-
Lack of efficacy	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description: Placebo control	
Reporting group title	VAY736 5 mg
Reporting group description: VAY736 low	
Reporting group title	VAY736 50 mg
Reporting group description: VAY736 medium	
Reporting group title	VAY736 300 mg
Reporting group description: VAY736 high	

Reporting group values	Placebo	VAY736 5 mg	VAY736 50 mg
Number of subjects	49	47	47
Age Categorical			
Randomized Set			
Units: Participants			
<=18 years	0	0	0
Between 18 and 65 years	45	37	42
>=65 years	4	10	5
Age Continuous			
Units: Years			
arithmetic mean	47.9	52.5	51.0
standard deviation	± 12.44	± 13.64	± 11.12
Sex: Female, Male			
Units: Participants			
Female	47	46	41
Male	2	1	6
Race/Ethnicity, Customized			
Units: Subjects			
Asian	4	3	10
Black or African American	0	1	0
White	44	42	37
Unknown	1	1	0

Reporting group values	VAY736 300 mg	Total	
Number of subjects	47	190	
Age Categorical			
Randomized Set			
Units: Participants			
<=18 years	0	0	
Between 18 and 65 years	39	163	
>=65 years	8	27	

Age Continuous Units: Years			
arithmetic mean	49.1		
standard deviation	± 15.41	-	
Sex: Female, Male Units: Participants			
Female	46	180	
Male	1	10	
Race/Ethnicity, Customized Units: Subjects			
Asian	5	22	
Black or African American	0	1	
White	42	165	
Unknown	0	2	

Subject analysis sets	
Subject analysis set title	Placebo - VAY150 mg
Subject analysis set type	Full analysis
Subject analysis set description: Placebo control	
Subject analysis set title	VAY736 300 mg - Placebo
Subject analysis set type	Full analysis
Subject analysis set description: VAY736 high	
Subject analysis set title	VAY736 300 mg - Placebo
Subject analysis set type	Full analysis
Subject analysis set description: VAY736 300 mg - Placebo	

Reporting group values	Placebo - VAY150 mg	VAY736 300 mg - Placebo	VAY736 300 mg - Placebo
Number of subjects	49	26	21
Age Categorical			
Randomized Set			
Units: Participants			
<=18 years	0	0	0
Between 18 and 65 years	0	0	0
>=65 years	0	0	0
Age Continuous Units: Years			
arithmetic mean	55.0	55.77	2.15
standard deviation	± 15.053	± 20.407	± 1.47
Sex: Female, Male Units: Participants			
Female			
Male			
Race/Ethnicity, Customized Units: Subjects			
Asian			
Black or African American			
White			

Unknown			

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Placebo control	
Reporting group title	VAY736 5 mg
Reporting group description: VAY736 low	
Reporting group title	VAY736 50 mg
Reporting group description: VAY736 medium	
Reporting group title	VAY736 300 mg
Reporting group description: VAY736 high	
Reporting group title	VAY736 150 mg
Reporting group description: Placebo in Period 2 and VAY736 150 mg in Period 3	
Reporting group title	VAY736 - Placebo 300 mg
Reporting group description: VAY736 300 mg in Period 2 and Placebo in Period 3	
Reporting group title	VAY736 300 mg - VAY736 300 mg
Reporting group description: VAY736 300 mg in Period 2 and Period 3	
Reporting group title	Placebo
Reporting group description: Placebo control	
Reporting group title	VAY736 5 mg
Reporting group description: VAY736 low	
Reporting group title	VAY736 50 mg
Reporting group description: VAY736 medium	
Reporting group title	VAY736 150 mg
Reporting group description: Placebo in Period 2 and VAY736 150 mg in Period 3	
Reporting group title	VAY736 300 mg
Reporting group description: VAY736 high	
Reporting group title	VAY736 - Placebo 300 mg
Reporting group description: VAY736 300 mg in Period 2 and Placebo in Period 3	
Reporting group title	VAY736 300 mg - VAY736 300 mg
Reporting group description: VAY736 300 mg in Period 2 and Period 3	
Subject analysis set title	Placebo - VAY150 mg
Subject analysis set type	Full analysis
Subject analysis set description: Placebo control	
Subject analysis set title	VAY736 300 mg - Placebo

Subject analysis set type	Full analysis
Subject analysis set description: VAY736 high	
Subject analysis set title	VAY736 300 mg - Placebo
Subject analysis set type	Full analysis
Subject analysis set description: VAY736 300 mg - Placebo	

Primary: Change from baseline in ESSDAI score at Week 24

End point title	Change from baseline in ESSDAI score at Week 24

End point description:

Dose response measured by change multi-dimensional disease activity as assessed by the physician.

Score range is 0-123. Higher scores on the EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) scale are associated with poorer health states

A negative change from baseline indicates improvement in disease status.

End point type	Primary
End point timeframe: Baseline, 24 weeks	

End point values	Placebo	VAY736 5 mg	VAY736 50 mg	VAY736 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	47	47	47
Units: Scores on a scale				
least squares mean (standard error)	-6.39 (± 0.808)	-5.64 (± 0.850)	-6.93 (± 0.836)	-8.30 (± 0.828)

Statistical analyses

Statistical analysis title	VAY736 5 mg
Comparison groups	Placebo v VAY736 5 mg
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5161
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.52
upper limit	3.02

Statistical analysis title	VAY736 300 mg
Comparison groups	Placebo v VAY736 300 mg
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0921
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-1.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.15
upper limit	0.32

Statistical analysis title	VAY736 50 mg
Comparison groups	Placebo v VAY736 50 mg
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6332
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-0.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	1.71

Secondary: Change from baseline in ESSDAI score at Weeks 4, 8, 12, and 16

End point title	Change from baseline in ESSDAI score at Weeks 4, 8, 12, and 16

End point description:

Dose response measured by change multi-dimensional disease activity as assessed by the physician.

Score range is 0-123. Higher scores on the EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) scale are associated with poorer health states

A negative change from baseline indicates improvement in disease status.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12, and 16

End point values	Placebo	VAY736 5 mg	VAY736 50 mg	VAY736 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	47	47	47
Units: Scores on a scale				
least squares mean (standard error)				
Week 4	-3.73 (± 0.626)	-2.28 (± 0.661)	-3.37 (± 0.638)	-4.53 (± 0.651)
Week 8	-4.13 (± 0.704)	-4.65 (± 0.733)	-4.73 (± 0.720)	-6.38 (± 0.717)
Week 12	-5.45 (± 0.721)	-4.89 (± 0.762)	-5.69 (± 0.739)	-6.64 (± 0.739)
Week 16	-6.08 (± 0.818)	-5.67 (± 0.852)	-6.17 (± 0.835)	-6.99 (± 0.836)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in ESSPRI score at Week 24

End point title	Change from baseline in ESSPRI score at Week 24

End point description:

Change in quality of life measure by patient reported outcome (PRO)

The EULAR Sjörgen's Syndrome Patient Reported Index (ESSPRI) is an established disease outcome measure for Sjögren’s syndrome that is calculated by averaging the scales for pain, fatigue and dryness. The total score is the mean score of the 3 scales and ranges between 0 and 10 with higher values indicating more severity of symptoms. A negative change from baseline is a favourable outcome.

End point type	Secondary

End point timeframe:

Baseline, 24 weeks

End point values	Placebo	VAY736 5 mg	VAY736 50 mg	VAY736 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	47	47	47
Units: Scores on a scale				
least squares mean (standard error)	-1.71 (± 0.288)	-1.39 (± 0.304)	-1.70 (± 0.301)	-1.77 (± 0.295)

Statistical analyses

Statistical analysis title	VAY736 5 mg
Comparison groups	Placebo v VAY736 5 mg

Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4457
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	0.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	1.13

Statistical analysis title	VAY736 50 mg
Comparison groups	Placebo v VAY736 50 mg
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.301
Method	Mixed models analysis
Parameter estimate	Least Square Mean Difference
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.79
upper limit	0.82

Statistical analysis title	VAY736 300 mg
Comparison groups	Placebo v VAY736 300 mg
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8858
Method	Mixed models analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.86
upper limit	0.74

Secondary: Change from baseline in ESSPRI score at Weeks 4, 8, 12 and 16

End point title	Change from baseline in ESSPRI score at Weeks 4, 8, 12 and 16

End point description:

Change in quality of life measure by patient reported outcome (PRO)

The EULAR Sjörgen's Syndrome Patient Reported Index (ESSPRI) is an established disease outcome measure for Sjögren's syndrome that is calculated by averaging the scales for pain, fatigue and dryness. The total score is the mean score of the 3 scales and ranges between 0 and 10 with higher values indicating more severity of symptoms. A negative change from baseline is a favourable outcome.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12 and 16

End point values	Placebo	VAY736 5 mg	VAY736 50 mg	VAY736 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	47	47	47
Units: Scores on a scale				
least squares mean (standard error)				
Week 4	-0.54 (± 0.236)	-0.67 (± 0.247)	-0.80 (± 0.241)	-0.88 (± 0.242)
Week 8	-0.94 (± 0.242)	-0.84 (± 0.255)	-1.06 (± 0.251)	-1.8 (± 0.248)
Week 12	-1.42 (± 0.265)	-1.36 (± 0.279)	-1.44 (± 0.273)	-1.23 (± 0.270)
Week 16	-1.77 (± 0.263)	-1.27 (± 0.275)	-1.55 (± 0.271)	-1.55 (± 0.270)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in FACIT-F score at Week 24

End point title	Change from baseline in FACIT-F score at Week 24

End point description:

Change in FACIT-F from baseline over 24 weeks as compared to placebo. The Functional Assessment of Chronic Illness Therapy-Fatigue Scale (FACIT-F v4) is a short, 13-item, easy-to-administer tool that measures an individual's level of fatigue during their usual daily activities over the previous week. The level of fatigue is measured on a four-point Likert scale (4 = not at all fatigued to 0 = very much fatigued). The global score ranges between 0 and 52, with higher scores indicating less fatigue.

End point type	Secondary

End point timeframe:

Baseline to 24 weeks

End point values	Placebo	VAY736 5 mg	VAY736 50 mg	VAY736 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	47	47	47
Units: Scores on a scale				
least squares mean (standard error)	9.05 (± 1.404)	7.12 (± 1.502)	6.48 (± 1.518)	9.36 (± 1.436)

Statistical analyses

Statistical analysis title	VAY736 5 mg
Comparison groups	Placebo v VAY736 5 mg
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3424
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-1.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.93
upper limit	2.07

Statistical analysis title	VAY736 300 mg
Comparison groups	Placebo v VAY736 300 mg
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.874
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	0.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.58
upper limit	4.2

Statistical analysis title	VAY736 50 mg
Comparison groups	Placebo v VAY736 50 mg

Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2092
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-2.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.58
upper limit	1.45

Secondary: Change from baseline in FACIT-F score at Weeks 4, 8, 12 and 16

End point title	Change from baseline in FACIT-F score at Weeks 4, 8, 12 and 16

End point description:

Change in FACIT-F from baseline as compared to placebo. The Functional Assessment of Chronic Illness Therapy-Fatigue Scale (FACIT-F v4) is a short, 13-item, easy-to-administer tool that measures an individual's level of fatigue during their usual daily activities over the previous week. The level of fatigue is measured on a four-point Likert scale (4 = not at all fatigued to 0 = very much fatigued). The global score ranges between 0 and 52, with higher scores indicating less fatigue.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12 and 16

End point values	Placebo	VAY736 5 mg	VAY736 50 mg	VAY736 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	42	39	46
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Week 4	3.78 (± 1.175)	6.32 (± 1.239)	3.12 (± 1.229)	3.39 (± 1.203)
Week 8	5.49 (± 1.222)	6.36 (± 1.297)	3.93 (± 1.303)	5.98 (± 1.250)
Week 12	6.25 (± 1.349)	8.17 (± 1.429)	5.73 (± 1.427)	6.05 (± 1.374)
Week 16	8.56 (± 1.284)	7.09 (± 1.357)	6.86 (± 1.359)	8.30 (± 1.318)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in salivary flow rate at Week 24

End point title	Change from baseline in salivary flow rate at Week 24

End point description:

Change from baseline in salivary flow rate (unstimulated and stimulated) at 24 weeks as compared to placebo.

Unstimulated saliva is a mix of serous and mucous secretions coming primarily from the submandibular and minor salivary glands. The parotid gland produces the largest volume of stimulated saliva. Stimulated saliva accounts for 80-90% of daily salivary production.

End point type	Secondary

End point timeframe:

Baseline, 24 weeks

End point values	Placebo	VAY736 5 mg	VAY736 50 mg	VAY736 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	47	47	47
Units: mL/min				
least squares mean (standard error)				
Stimulated	0.05 (± 0.067)	0.16 (± 0.074)	0.18 (± 0.071)	0.25 (± 0.98)
Unstimulated	0.12 (± 0.20)	0.12 (± 0.17)	0.10 (± 0.13)	0.25 (± 0.069)

Statistical analyses

Statistical analysis title	VAY736 5 mg
Statistical analysis description: Stimulated	
Comparison groups	Placebo v VAY736 5 mg
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.271
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.08
upper limit	0.3

Statistical analysis title	VAY736 50 mg
Statistical analysis description: Stimulated	
Comparison groups	Placebo v VAY736 50 mg

Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1618
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	0.32

Statistical analysis title	VAY736 300 mg
Statistical analysis description: Stimulated	
Comparison groups	Placebo v VAY736 300 mg
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0374
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.01
upper limit	0.38

Statistical analysis title	VAY736 5 mg
Statistical analysis description: Unstimulated	
Comparison groups	Placebo v VAY736 5 mg
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9559
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.09
upper limit	0.09

Statistical analysis title	VAY736 50 mg
Statistical analysis description: Unstimulated	
Comparison groups	Placebo v VAY736 50 mg
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.929
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.09
upper limit	0.08

Statistical analysis title	VAY736 300 mg
Statistical analysis description: Unstimulated	
Comparison groups	Placebo v VAY736 300 mg
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7276
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.07

Secondary: Change from SF-36 physical component (PCS) and mental component (MCS) at Week 24

End point title	Change from SF-36 physical component (PCS) and mental component (MCS) at Week 24

End point description:

Change from SF-36 physical component (PCS) and mental component (MCS) from baseline over 24 weeks as compared to placebo

The SF36 includes 8 scale scores (physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health) and two summary scores, the physical and mental component scores. The first four and last four scales comprise physical and mental

component scores, respectively. The range of scores of the physical component (PCS) and mental component (MCS) is 0 (lowest or worst possible level of functioning) to 100 (highest or best possible level of functioning).

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Placebo	VAY736 5 mg	VAY736 50 mg	VAY736 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	47	47	47
Units: Scores on a scale				
least squares mean (standard error)				
Mental Component Score	4.63 (± 1.259)	3.61 (± 1.350)	5.31 (± 1.367)	5.63 (± 1.286)
Physical Component Score	3.66 (± 0.952)	4.79 (± 1.019)	2.66 (± 1.026)	5.50 (± 0.972)

Statistical analyses

Statistical analysis title	VAY736 5 mg
Statistical analysis description: Mental Component Score	
Comparison groups	Placebo v VAY736 5 mg
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5768
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.61
upper limit	2.57

Statistical analysis title	VAY736 50 mg
Statistical analysis description: Mental Component Score	
Comparison groups	Placebo v VAY736 50 mg

Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7113
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.93
upper limit	4.28

Statistical analysis title	VAY736 300 mg
Statistical analysis description: Mental Component Score	
Comparison groups	Placebo v VAY736 300 mg
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5722
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.49
upper limit	4.48

Statistical analysis title	VAY736 5 mg
Statistical analysis description: Physical Component Score	
Comparison groups	Placebo v VAY736 5 mg
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4138
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	1.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.59
upper limit	3.83

Statistical analysis title	VAY736 50 mg
Statistical analysis description: Physical Component Score	
Comparison groups	Placebo v VAY736 50 mg
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4663
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.72
upper limit	1.71

Statistical analysis title	VAY736 300 mg
Statistical analysis description: Physical Component Score	
Comparison groups	Placebo v VAY736 300 mg
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1694
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	1.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.79
upper limit	4.47

Secondary: Change from SF-36 physical component (PCS) and mental component (MCS) from Baseline to Weeks 4, 8, 12 and 16

End point title	Change from SF-36 physical component (PCS) and mental component (MCS) from Baseline to Weeks 4, 8, 12 and 16

End point description:

Change from SF-36 physical component (PCS) and mental component (MCS) from baseline over to 16 weeks as compared to placebo

The SF36 includes 8 scale scores (physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health) and two summary scores, the physical and mental component scores. The first four and last four scales comprise physical and mental

component scores, respectively. The range of scores of the physical component (PCS) and mental component (MCS) is 0 (lowest or worst possible level of functioning) to 100 (highest or best possible level of functioning).

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12 and 16

End point values	Placebo	VAY736 5 mg	VAY736 50 mg	VAY736 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	47	47	47
Units: Scores on a scale				
least squares mean (standard error)				
Week 4 - Mental Component Score	0.49 (± 1.091)	1.89 (± 1.151)	2.46 (± 1.149)	2.18 (± 1.116)
Week 8 - Mental Component Score	2.65 (± 2.267)	3.80 (± 1.341)	4.65 (± 1.363)	3.35 (± 1.294)
Week 12 - Mental Component Score	2.89 (± 1.188)	5.42 (± 1.264)	3.94 (± 1.265)	4.59 (± 1.207)
Week 16 - Mental Component Score	4.60 (± 1.214)	3.00 (± 1.281)	5.57 (± 1.291)	5.46 (± 1.247)
Week 4 - Physical Component Score	3.35 (± 0.844)	3.94 (± 0.889)	1.14 (± 0.878)	1.98 (± 0.863)
Week 8 - Physical Component Score	3.83 (± 0.894)	4.56 (± 0.949)	3.48 (± 0.941)	3.47 (± 0.909)
Week 12 - Physical Component Score	3.83 (± 0.894)	4.56 (± 0.949)	3.48 (± 0.941)	3.47 (± 0.909)
Week 16 - Physical Component Score	4.72 (± 0.968)	4.67 (± 1.020)	3.32 (± 1.021)	4.57 (± 0.993)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in PhGA of patient’s overall disease activity using Patient Visual Analog Scale (VAS) at 24 weeks

End point title	Change from baseline in PhGA of patient’s overall disease activity using Patient Visual Analog Scale (VAS) at 24 weeks

End point description:

Change from baseline in PhGA of patient’s overall disease activity (recorded by VAS) over 24 weeks as compared to placebo

Physician global assessment of overall disease activity (PhGA) was performed using a 100 mm visual analogue scale (VAS) ranging from no disease activity (score 0) to maximal disease activity (score 100), after the question “Considering all the ways the disease affects your patient, draw a line on the scale for how well his or her condition is today”.

A negative change from baseline is a favourable outcome.

End point type	Secondary

End point timeframe:

Baseline, 24 weeks

End point values	Placebo	VAY736 5 mg	VAY736 50 mg	VAY736 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	47	47	47
Units: Scores on a scale				
least squares mean (standard error)	-23.64 (± 2.601)	-27.81 (± 2.751)	-28.13 (± 2.700)	-31.99 (± 2.630)

Statistical analyses

Statistical analysis title	VAY736 5 mg
Comparison groups	Placebo v VAY736 5 mg
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2671
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-4.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.56
upper limit	3.22

Statistical analysis title	VAY736 50 mg
Comparison groups	Placebo v VAY736 50 mg
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2248
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-4.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.78
upper limit	2.79

Statistical analysis title	VAY736 300 mg
Comparison groups	Placebo v VAY736 300 mg

Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0224
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-8.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.51
upper limit	-1.2

Secondary: Change from baseline in PhGA of patient's overall disease activity using Patient Visual Analog Scale (VAS) at Weeks 4, 8, 12 and 16

End point title	Change from baseline in PhGA of patient's overall disease activity using Patient Visual Analog Scale (VAS) at Weeks 4, 8, 12 and 16

End point description:

Change from baseline in PhGA of patient's overall disease activity (recorded by VAS) as compared to placebo

Change from baseline in PhGA of patient's overall disease activity (recorded by VAS) over 16 weeks as compared to placebo

Physician global assessment of overall disease activity (PhGA) was performed using a 100 mm visual analogue scale (VAS) ranging from no disease activity (score 0) to maximal disease activity (score 100), after the question "Considering all the ways the disease affects your patient, draw a line on the scale for how well his or her condition is today".

A negative change from baseline is a favourable outcome.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12 and 16

End point values	Placebo	VAY736 5 mg	VAY736 50 mg	VAY736 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	47	47	47
Units: Scores on a scale				
least squares mean (standard error)				
Week 4	-12.49 (± 2.327)	-10.50 (± 2.445)	-12.38 (± 2.361)	-18.67 (± 2.367)
Week 8	-18.54 (± 2.239)	-16.53 (± 2.338)	-22.12 (± 2.374)	-24.85 (± 2.289)
Week 12	-21.01 (± 2.299)	-20.72 (± 2.413)	-25.35 (± 2.341)	-27.25 (± 2.305)
Week 16	-19.44 (± 2.572)	-24.49 (± 2.687)	-24.77 (± 2.676)	-25.77 (± 2.633)

Statistical analyses

No statistical analyses for this end point

Secondary: PaGA Score at Weeks 4, 8, 12, 16 and 24

End point title	PaGA Score at Weeks 4, 8, 12, 16 and 24

End point description:

Patient global assessment (PaGA) Score at Weeks 4, 8, 12, 16 and 24

The PaGA of disease activity was performed using a 100 mm Visual Analog Scale (VAS) ranging from 0 (no disease activity) to 100 (maximal disease activity), in response to the question "Considering all the ways Sjögren's syndrome affects you, please draw a line on the scale to indicate how well you are doing today".

End point type	Secondary

End point timeframe:

Weeks 4, 8, 12, 16 and 24

End point values	Placebo	VAY736 5 mg	VAY736 50 mg	VAY736 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	47	47	47
Units: Scores on a scale				
least squares mean (standard error)				
Week 4	-9.42 (± 2.850)	-10.02 (± 2.992)	-5.96 (± 2.969)	-8.96 (± 2.906)
Week 8	-9.74 (± 3.035)	-11.48 (± 3.214)	-8.70 (± 3.271)	-15.27 (± 3.091)
Week 12	-11.45 (± 3.064)	-17.51 (± 3.244)	-11.73 (± 3.234)	-13.57 (± 3.105)
Week 16	-16.26 (± 3.194)	-17.56 (± 3.361)	-14.86 (± 3.375)	-15.78 (± 3.271)
Week 24	-15.11 (± 3.405)	-12.83 (± 3.648)	-11.85 (± 3.704)	-19.87 (± 3.470)

Statistical analyses

Statistical analysis title	VAY736 5 mg

Statistical analysis description:

Baseline, Week 24

Comparison groups	Placebo v VAY736 5 mg

Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6457
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	2.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.46
upper limit	12

Statistical analysis title	VAY736 300 mg
Comparison groups	Placebo v VAY736 300 mg
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 95
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-4.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.21
upper limit	4.68

Statistical analysis title	VAY736 50 mg
Statistical analysis description: Baseline, Week 24	
Comparison groups	Placebo v VAY736 50 mg
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5132
Method	LS Mean Difference
Parameter estimate	LS Mean Difference
Point estimate	3.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.55
upper limit	13.06

Secondary: Time to Recovery to baseline like values for B-cell counts

End point title	Time to Recovery to baseline like values for B-cell counts[1]

End point description:

Kaplan-Meier Analysis for Time to Recovery to Baseline like Values (defined as at least 80% of baseline counts or ≥ 50 cells/µL) for B-cell counts – Entire Study (FAS)

VAY736 300 mg - Placebo includes patients who discontinued in Period 2 and entered Period 4 directly and patients who completed Period 2 and were re-randomized to placebo.

End point type	Secondary

End point timeframe:

Week 24; and then to last dose of administration up to a maximum of 2 years

Notes:

[1] - 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: No stats analysis were planned.

End point values	VAY736 5 mg	VAY736 50 mg	Placebo - VAY150 mg	VAY736 300 mg - Placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	47	47	49	26
Units: months				
median (confidence interval 95%)	3.8 (2.7 to 5.2)	4.8 (4.7 to 6.6)	6.8 (5.0 to 9.2)	8.4 (6.8 to 9.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in whole blood CD19+ B-cell counts. Units: percent change from baseline at Week 24

End point title	Change from baseline in whole blood CD19+ B-cell counts. Units: percent change from baseline at Week 24[2]

End point description:

Change from baseline in whole blood CD19+ B-cell counts. Units: percent change from baseline

VAY736 300 mg - Placebo includes patients who discontinued in Period 2 and entered Period 4 directly and patients who completed Period 2 and were re-randomized to placebo.

Baseline is defined as the last assessment performed on or prior to the date of administration of the first dose of study treatment. Only patients with baseline measurement and at least one measurement post-baseline were included.

End point type	Secondary

End point timeframe:

Baseline, Week 24

Notes:

[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: No stats analysis were planned.

End point values	VAY736 5 mg	VAY736 50 mg	Placebo - VAY150 mg	VAY736 300 mg - Placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	47	47	49	26
Units: pg/mL				
least squares mean (standard error)	150.36 (± 16.229)	241.14 (± 16.040)	-1.17 (± 15.053)	265.77 (± 20.407)

Statistical analyses

No statistical analyses for this end point

Secondary: Peak serum concentration of VAY736

End point title	Peak serum concentration of VAY736[3]

End point description:

Pharmacokinetic Concentrations

This outcome only applies to patients who received at least one dose of VAY739 (so not applicable to placebo)

End point type	Secondary

End point timeframe:

baseline to week 24

Notes:

[3] - 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: No stats analysis were planned.

End point values	VAY736 5 mg	VAY736 50 mg	VAY736 300 mg	VAY736 300 mg - Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	47	47	4	21
Units: ug/mL				
arithmetic mean (standard deviation)	0.0747 (± 0.203)	0.475 (± 0.380)	1.46 (± 0.596)	2.15 (± 1.47)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
AEs were collected from first dose of study treatment until end of study treatment at week 24 and then up to 28 weeks	
Adverse event reporting additional description:	
Adverse Events (AEs) are any untoward sign or symptom that occurs during the study treatment	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Not relevant to this analysis.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 January 2017	The main purpose of this global amendment was to remove inconsistencies and provide clarifications. At the time of this Amendment no patients had been screened or enrolled in the study.
07 January 2020	As of 16-Dec-2019, the study was fully enrolled and the primary efficacy analysis (when all randomized patients reached Week 24) had been performed. The purpose of this global amendment was to incorporate an additional analysis (Week 52) for reporting study results (interim Clinical Study Report) prior to the final study analysis.
22 May 2020	The main purpose of this global amendment was to: a) Remove the Inclusion Criterion of a mandatory salivary/lacrimal gland biopsy result confirming primary Sjögren's syndrome diagnosis prior to baseline visit; b) Revise the Exclusion Criterion to allow background therapy with azathioprine while on study treatment, for patients who had been treated with a stable dose for at least 3 months prior to randomization; c) Remove the Exclusion Criterion related to the requirement of using male contraception by male study participants; d) Provide more detailed guidance on recommended time window for use of artificial tears, artificial saliva and other salivary stimulants (e.g., cevimeline, pilocarpine) prior to performing the study assessments; e) Revise the timepoint of Inclusion Criterion requirement for ESSDAI score of 6 to be met at Screening period instead of Baseline; f) Add optional collection of the archival biopsy slides from the time of diagnosis for digital copy (scanning) and exploratory analysis; g) Revise the statistical section to remove analyses of exploratory nature and to clarify points for consistency. The study was initiated in Jun-2017 and as of 23-Mar-2018, 47 patients had been randomized.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported