Clinical trial results:
A Phase II, Randomized, Multi-Center, Double-Blind, Placebo Controlled Study to Evaluate the Efficacy and Safety of BMS-931699 (lulizumab) or BMS-986142 in Subjects with Moderate to Severe Primary Sjogren's Syndrome

Summary

EudraCT number	2016-000101-37
Trial protocol	GR IT
Global end of trial date	24 July 2017

Results information

Result version number	v1 (current)
This version publication date	09 August 2018
First version publication date	09 August 2018

Trial information

Trial identification

Sponsor protocol code	IM128-035

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02843659
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, EU Study Start-Up Unit, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.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	24 July 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 July 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this trial was to evaluate the efficacy of treatment with either lulizumab or BMS-986142 versus placebo in subjects with moderate to severe pSS as measured by the change from baseline in EULAR SS Disease Activity Index (ESSDAI) at Week 12 between active treatment arms (lulizumab or BMS-986142, respectively) and the placebo arm

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 October 2016
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	Russian Federation: 1
Country: Number of subjects enrolled	Mexico: 10
Country: Number of subjects enrolled	Puerto Rico: 2
Country: Number of subjects enrolled	United States: 4
Country: Number of subjects enrolled	Peru: 1
Worldwide total number of subjects	18
EEA total number of subjects	0

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)	15
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

45 subjects enrolled, 18 subjects were randomized/treated. 15 subjects didn’t complete the treatment period. The study was terminated and the remaining 15 randomized subjects who had not yet completed the double-blind period entered the follow-up period. Of the 15 subjects who entered the follow-up period, 12 did not complete the follow-up period

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	BMS-931699/lulizumab injection

Arm description:

(12.5mg/vial, 12.5mg/mL) for subcutaneous (SC)

Arm type	Experimental
Investigational medicinal product name	Lulizumab
Investigational medicinal product code	
Other name	BMS-931699
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Subcutaneous weekly injection

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subcutaneous weekly injection + daily oral placebo tablets

Arm title	BMS-986142 50 mg tablet (round) or 150 mg tablet (oval)

Arm description:

For oral administration, 350 mg

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

Dosage and administration details:

Daily oral tablets + subcutaneous placebo (weekly) injection

Investigational medicinal product name	BMS-986142
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Daily oral tablets + subcutaneous placebo (weekly) injection

Arm title	Placebo

Arm description:

For BMS-986142 50 mg tablet (round) or 150 mg tablet

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

Dosage and administration details:

Weekly subcutaneous placebo injection +daily oral placebo tablets

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Other use

Dosage and administration details:

Weekly subcutaneous placebo injection +daily oral placebo tablets

Number of subjects in period 1	BMS-931699/lulizumab injection	BMS-986142 50 mg tablet (round) or 150 mg tablet (oval)	Placebo
Started	5	6	7
Completed	1	0	2
Not completed	4	6	5
Subject Withdrew Consent	-	-	1
Adverse event, non-fatal	-	1	-
Administrative Reason by Sponsor	4	5	4

Baseline characteristics

Reporting groups	
Reporting group title	BMS-931699/lulizumab injection
Reporting group description: (12.5mg/vial, 12.5mg/mL) for subcutaneous (SC)	
Reporting group title	BMS-986142 50 mg tablet (round) or 150 mg tablet (oval)
Reporting group description: For oral administration, 350 mg	
Reporting group title	Placebo
Reporting group description: For BMS-986142 50 mg tablet (round) or 150 mg tablet	

Reporting group values	BMS-931699/lulizumab injection	BMS-986142 50 mg tablet (round) or 150 mg tablet (oval)	Placebo
Number of subjects	5	6	7
Age categorical			
Subjects			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	5	5	5
From 65-84 years	0	1	2
85 years and over	0	0	0
Age Continuous			
Units: months			
arithmetic mean	49.2	51.2	52.6
standard deviation	± 11.34	± 8.77	± 13.30
Sex: Female, Male			
Units: Subjects			
Female	5	6	7
Male	0	0	0
Race/Ethnicity, Customized			
Units: Subjects			
White|	4	4	7
Black or African American|	0	0	0
Asian|	0	0	0
American Indian or Alaska Native|	0	0	0
Native Hawaiian or Other Pacific Islander|	0	0	0
Other|	1	2	0

Reporting group values	Total		
Number of subjects	18		

Age categorical			
Subjects			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	15		
From 65-84 years	3		
85 years and over	0		
Age Continuous			
Units: months			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Units: Subjects			
Female	18		
Male	0		
Race/Ethnicity, Customized			
Units: Subjects			
White|	15		
Black or African American|	0		
Asian|	0		
American Indian or Alaska Native|	0		
Native Hawaiian or Other Pacific Islander|	0		
Other|	3		

End points

End points reporting groups

Reporting group title	BMS-931699/lulizumab injection
Reporting group description: (12.5mg/vial, 12.5mg/mL) for subcutaneous (SC)	
Reporting group title	BMS-986142 50 mg tablet (round) or 150 mg tablet (oval)
Reporting group description: For oral administration, 350 mg	
Reporting group title	Placebo
Reporting group description: For BMS-986142 50 mg tablet (round) or 150 mg tablet	

Primary: Mean change from baseline in ESSDAI

End point title	Mean change from baseline in ESSDAI[1]

End point description:

The ESSDAI is a clinical index that measures Sjogren's syndrome disease activity. A physician scores the disease activity level of twelve organ-specific domains in 3 or 4 levels according to their severity. For example, for no disease activity the domain score equals 0 and for high disease activity the domain score equals 3 or 4. Each domain is assigned a weight between 1 and 6, and the domain score is multiplied by the domain weight. The sum of the weighted domain scores is the overall score, which can range from 0 to 123. A higher score indicates more disease activity. Change from baseline was computed as the value at Week 24 minus the baseline value. A negative value in change from baseline indicates an improvement and a positive value indicates worsening

End point type	Primary

End point timeframe:

At baseline and week 12

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No summary statistics were planned.

End point values	BMS-931699/lulizumab injection	BMS-986142 50 mg tablet (round) or 150 mg tablet (oval)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[2]	0[3]	0[4]	
Units: subjects				
arithmetic mean (standard error)	()	()	()	

Notes:

[2] - This study was terminated early

[3] - This study was terminated early

[4] - This study was terminated early

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change from baseline in ESSDAI scores at Week 4 and Week 8

End point title	Mean Change from baseline in ESSDAI scores at Week 4 and

	Week 8

End point description:

The ESSDAI is a clinical index that measures Sjogren’s syndrome disease activity. A physician scores the disease activity level of twelve organ-specific domains in 3 or 4 levels according to their severity. For example, for no disease activity the domain score equals 0 and for high disease activity the domain score equals 3 or 4. Each domain is assigned a weight between 1 and 6, and the domain score is multiplied by the domain weight. The sum of the weighted domain scores is the overall score, which can range from 0 to 123. A higher score indicates more disease activity. Change from baseline was computed as the value at Week 24 minus the baseline value. A negative value in change from baseline indicates an improvement and a positive value indicates worsening

End point type	Secondary

End point timeframe:

At baseline, week 4 and week 8

End point values	BMS-931699/lulizumab injection	BMS-986142 50 mg tablet (round) or 150 mg tablet (oval)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[5]	0[6]	0[7]	
Units: subjects				
arithmetic mean (standard deviation)				
Week 4|	()	()	()	
Week 8|	()	()	()	

Notes:

[5] - This study was terminated early

[6] - This study was terminated early

[7] - This study was terminated early

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change from baseline in ESSPRI Score at week 4, week 8, and week 12.

End point title	Mean Change from baseline in ESSPRI Score at week 4, week 8, and week 12.

End point description:

ESSPRI, also known as EULAR Sjogren's Syndrome Patient Reported Index, measures subjective symptoms of dryness, pain and fatigue. It uses 0-10 numerical scales, one for each domain. The weight of the domains is identical, and the final score is the mean score of the 3 domains.

End point type	Secondary

End point timeframe:

At baseline, week 4, week 8, and week 12

End point values	BMS-931699/lulizumab injection	BMS-986142 50 mg tablet (round) or 150 mg tablet (oval)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[8]	0[9]	0[10]	
Units: subjects				
arithmetic mean (standard deviation)				
Week 4|	()	()	()	
Week 8|	()	()	()	
Week 12|	()	()	()	

Notes:

[8] - This study was terminated early

[9] - This study was terminated early

[10] - This study was terminated early

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects with a > = 3 point improvement from baseline in ESSDAI at Week 12

End point title	Proportion of subjects with a > = 3 point improvement from baseline in ESSDAI at Week 12

End point description:

The ESSDAI is a clinical index that measures Sjogren's syndrome disease activity. A physician scores the disease activity level of twelve organ-specific domains in 3 or 4 levels according to their severity. For example, for no disease activity the domain score equals 0 and for high disease activity the domain score equals 3 or 4. Each domain is assigned a weight between 1 and 6, and the domain score is multiplied by the domain weight. The sum of the weighted domain scores is the overall score, which can range from 0 to 123. A higher score indicates more disease activity. Change from baseline was computed as the value at Week 24 minus the baseline value. A negative value in change from baseline indicates an improvement and a positive value indicates worsening

End point type	Secondary

End point timeframe:

At week 12

End point values	BMS-931699/lulizumab injection	BMS-986142 50 mg tablet (round) or 150 mg tablet (oval)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[11]	0[12]	0[13]	
Units: subjects				

Notes:

[11] - This study was terminated early

[12] - This study was terminated early

[13] - This study was terminated early

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects with both >= 3 points improvement in ESSDAI and >= 1 point improvement in ESSPRI from baseline at Week 12

End point title	Proportion of subjects with both >= 3 points improvement in ESSDAI and >= 1 point improvement in ESSPRI from baseline at Week 12

End point description:

The ESSDAI is a clinical index that measures Sjogren's syndrome disease activity. A physician scores the disease activity level of twelve organ-specific domains in 3 or 4 levels according to their severity. For example, for no disease activity the domain score equals 0 and for high disease activity the domain score equals 3 or 4. Each domain is assigned a weight between 1 and 6, and the domain score is multiplied by the domain weight. The sum of the weighted domain scores is the overall score, which can range from 0 to 123. A higher score indicates more disease activity. Change from baseline was computed as the value at Week 24 minus the baseline value. A negative value in change from baseline indicates an improvement and a positive value indicates worsening

End point type	Secondary

End point timeframe:

At week 12

End point values	BMS-931699/lulizumab injection	BMS-986142 50 mg tablet (round) or 150 mg tablet (oval)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[14]	0[15]	0[16]	
Units: subjects				

Notes:

[14] - This study was terminated early

[15] - This study was terminated early

[16] - This study was terminated early

Statistical analyses

No statistical analyses for this end point

Secondary: Proportions of subjects with >=1 point of improvement from baseline in ESSPRI

End point title	Proportions of subjects with >=1 point of improvement from baseline in ESSPRI

End point description:

ESSPRI, also known as EULAR Sjogren's Syndrome Patient Reported Index, measures subjective symptoms of dryness, pain and fatigue. It uses 0-10 numerical scales, one for each domain. The weight of the domains is identical, and the final score is the mean score of the 3 domains

End point type	Secondary

End point timeframe:

At week 12

End point values	BMS-931699/lulizumab injection	BMS-986142 50 mg tablet (round) or 150 mg tablet (oval)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[17]	0[18]	0[19]	
Units: subjects				

Notes:

[17] - This study was terminated early

[18] - This study was terminated early

[19] - This study was terminated early

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change in baseline in ESSPRI individual component of dryness

End point title	Mean Change in baseline in ESSPRI individual component of dryness

End point description:

ESSPRI, also known as EULAR Sjogren's Syndrome Patient Reported Index, measures subjective symptoms of dryness, pain and fatigue. It uses 0-10 numerical scales, one for each domain. The weight of the domains is identical, and the final score is the mean score of the 3 domains

End point type	Secondary

End point timeframe:

At baseline, week 4, week 8, and week 12

End point values	BMS-931699/lulizumab injection	BMS-986142 50 mg tablet (round) or 150 mg tablet (oval)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[20]	0[21]	0[22]	
Units: subjects				
arithmetic mean (standard deviation)				
Week 4|	()	()	()	
Week 8|	()	()	()	
Week 12|	()	()	()	

Notes:

[20] - This study was terminated early

[21] - This study was terminated early

[22] - This study was terminated early

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change in baseline in ESSPRI individual component of fatigue

End point title	Mean Change in baseline in ESSPRI individual component of fatigue

End point description:

ESSPRI, also known as EULAR Sjogren's Syndrome Patient Reported Index, measures subjective symptoms of dryness, pain and fatigue. It uses 0-10 numerical scales, one for each domain. The weight of the domains is identical, and the final score is the mean score of the 3 domains

End point type	Secondary

End point timeframe:

At baseline, week 4, week 8, and week 12

End point values	BMS-931699/lulizumab injection	BMS-986142 50 mg tablet (round) or 150 mg tablet (oval)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[23]	0[24]	0[25]	
Units: subjects				
arithmetic mean (standard deviation)				
Week 4|	()	()	()	
Week 8|	()	()	()	
Week 12|	()	()	()	

Notes:

[23] - This study was terminated early

[24] - This study was terminated early

[25] - This study was terminated early

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change in baseline in ESSPRI individual component of pain

End point title	Mean Change in baseline in ESSPRI individual component of pain

End point description:

ESSPRI, also known as EULAR Sjogren's Syndrome Patient Reported Index, measures subjective symptoms of dryness, pain and fatigue. It uses 0-10 numerical scales, one for each domain. The weight of the domains is identical, and the final score is the mean score of the 3 domains

End point type	Secondary

End point timeframe:

At baseline, week 4, week 8, and week 12

End point values	BMS-931699/lulizumab injection	BMS-986142 50 mg tablet (round) or 150 mg tablet (oval)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[26]	0[27]	0[28]	
Units: subjects				
arithmetic mean (standard deviation)				
Week 4|	()	()	()	

Week 8|	()	()	()	
Week 12|	()	()	()	

Notes:

[26] - This study was terminated early

[27] - This study was terminated early

[28] - This study was terminated early

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline in unstimulated salivary flow rate

End point title	Mean change from baseline in unstimulated salivary flow rate

End point description:

Serum and saliva biomarkers (collected from samples obtained during unstimulated and stimulated salivary flow assessments) were measured to determine the potential PD effect of BMS-931699 and BMS-986142 on disease-related protein analytes. These assessments included, but were not limited to, the detection of cytokines and other protein analytes by immunoassays and/or mass spectrometry proteomic profiling.

End point type	Secondary

End point timeframe:

At baseline, week 4, week 8, and week 12

End point values	BMS-931699/lulizumab injection	BMS-986142 50 mg tablet (round) or 150 mg tablet (oval)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[29]	0[30]	0[31]	
Units: subjects				
arithmetic mean (standard deviation)				
Week 4|	()	()	()	
Week 8|	()	()	()	
Week 12|	()	()	()	

Notes:

[29] - This study was terminated early

[30] - This study was terminated early

[31] - This study was terminated early

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline in stimulated salivary flow rate

End point title	Mean change from baseline in stimulated salivary flow rate

End point description:

Serum and saliva biomarkers (collected from samples obtained during unstimulated and stimulated salivary flow assessments) were measured to determine the potential PD effect of BMS-931699 and BMS-986142 on disease-related protein analytes. These assessments included, but were not limited to, the detection of cytokines and other protein analytes by immunoassays and/or mass spectrometry proteomic profiling.

End point type	Secondary

End point timeframe:

At baseline, week 4, week 8, and week 12

End point values	BMS-931699/lulizumab injection	BMS-986142 50 mg tablet (round) or 150 mg tablet (oval)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[32]	0[33]	0[34]	
Units: subjects				
arithmetic mean (standard deviation)				
Week 4|	()	()	()	
Week 8|	()	()	()	
Week 12|	()	()	()	

Notes:

[32] - This study was terminated early

[33] - This study was terminated early

[34] - This study was terminated early

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline in ocular surface staining

End point title	Mean change from baseline in ocular surface staining

End point description:

The test was performed by instillation of fluorescein dye and either lissamine green or Rose bengal dye to stain the cornea and conjunctiva, respectively. After instilling the dye, the ocular surface was examined through a slit lamp (biomicroscope).

End point type	Secondary

End point timeframe:

At baseline, week 4, week 8, and week 12

End point values	BMS-931699/lulizumab injection	BMS-986142 50 mg tablet (round) or 150 mg tablet (oval)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[35]	0[36]	0[37]	
Units: subjects				
arithmetic mean (standard deviation)				
Week 4|	()	()	()	
Week 8|	()	()	()	
Week 12|	()	()	()	

Notes:

[35] - This study was terminated early

[36] - This study was terminated early

[37] - This study was terminated early

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline in Schrimer's test

End point title	Mean change from baseline in Schrimer's test

End point description:

The test (without anaesthesia) was performed by placing a narrow calibrated filter-paper strip in the inferior cul-de-sac of each eye. Aqueous tear production was measured by the length in millimeters that the strip wets during the 5 minute test period

End point type	Secondary

End point timeframe:

At baseline, week 4, week 8, and week 12

End point values	BMS-931699/lulizumab injection	BMS-986142 50 mg tablet (round) or 150 mg tablet (oval)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[38]	0[39]	0[40]	
Units: subjects				
arithmetic mean (standard deviation)				
Week 4|	()	()	()	
Week 8|	()	()	()	
Week 12|	()	()	()	

Notes:

[38] - This study was terminated early

[39] - This study was terminated early

[40] - This study was terminated early

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline in the tear break-up time test

End point title	Mean change from baseline in the tear break-up time test

End point description:

Determined by instilling fluorescein dye and evaluating the stability of the pre-corneal tear film. After several blinks, the tear film is examined using a broad beam of the slit-lamp (biomicroscope) with a cobalt blue filter. The TBUT, defined as the time in seconds between the subjects's last blink and the first appearance of a random dry spot on the corneal surface, is measured 3 times and the mean value is recorded.

End point type	Secondary

End point timeframe:

At baseline, week 4, week 8, and week 12

End point values	BMS-931699/lulizumab injection	BMS-986142 50 mg tablet (round) or 150 mg tablet (oval)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[41]	0[42]	0[43]	
Units: subjects				
arithmetic mean (standard deviation)				
Week 4|	()	()	()	
Week 8|	()	()	()	
Week 12|	()	()	()	

Notes:

[41] - This study was terminated early

[42] - This study was terminated early

[43] - This study was terminated early

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline in numeric rating scale (NRS) for mouth, eye and vaginal dryness

End point title	Mean change from baseline in numeric rating scale (NRS) for mouth, eye and vaginal dryness

End point description:

The Numeric Rating Scale (NRS-11) is an 11-point scale for patient self-reporting of pain. 0 = No Pain, 1–3 = Mild Pain(nagging, annoying, interfering little with ADLs), 4–6 = Moderate Pain (interferes significantly with ADLs), 7–10 = Severe Pain (disabling; unable to perform ADLs)

End point type	Secondary

End point timeframe:

At baseline, at week 2, week 4, week 6, week 8, week 10, week 12, and week 18

End point values	BMS-931699/lulizumab injection	BMS-986142 50 mg tablet (round) or 150 mg tablet (oval)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[44]	0[45]	0[46]	
Units: subjects				
arithmetic mean (standard deviation)				
Week 2|	()	()	()	
Week 4|	()	()	()	
Week 6|	()	()	()	
Week 8|	()	()	()	
Week 10|	()	()	()	

Week 12|	()	()	()	
Week 18|	()	()	()	

Notes:

[44] - This study was terminated early

[45] - This study was terminated early

[46] - This study was terminated early

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline in subject global assessment of disease activity (SubGDA)

End point title	Mean change from baseline in subject global assessment of disease activity (SubGDA)

End point description:

The study was terminated for administrative reasons after 18 subjects were enrolled. Of these, only 3 subjects – 2 in the placebo arm, and 1 in the lulizumab 12.5 mg arm reached the end of treatment period at Wk 12. Since it is not appropriate to summarize efficacy in treatment arms with so few observations, no summaries were performed

End point type	Secondary

End point timeframe:

At baseline, week 2, week 4, week 6, week 8, week 10, week 12, and week 18

End point values	BMS-931699/lulizumab injection	BMS-986142 50 mg tablet (round) or 150 mg tablet (oval)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[47]	0[48]	0[49]	
Units: subjects				
arithmetic mean (standard error)				
Week 2|	()	()	()	
Week 4|	()	()	()	
Week 6|	()	()	()	
Week 8|	()	()	()	
Week 10|	()	()	()	
Week 12|	()	()	()	
Week 18|	()	()	()	

Notes:

[47] - This study was terminated early

[48] - This study was terminated early

[49] - This study was terminated early

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change form baseline in physician global assessment of disease activity (phyGDA)

End point title	Mean change form baseline in physician global assessment of

	disease activity (phyGDA)

End point description:

The investigator's or physician's overall assessment of disease activity from 0-10 cm VAS scale with 0 being no disease and 10 cm being most severe disease.

End point type	Secondary

End point timeframe:

At baseline, week 2, week 4, week 6, week 8, week 10, week 12, and week 18

End point values	BMS-931699/lulizumab injection	BMS-986142 50 mg tablet (round) or 150 mg tablet (oval)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[50]	0[51]	0[52]	
Units: subjects				
arithmetic mean (standard deviation)				
Week 2|	()	()	()	
Week 4|	()	()	()	
Week 6|	()	()	()	
Week 8|	()	()	()	
Week 10|	()	()	()	
Week 12|	()	()	()	
Week 18|	()	()	()	

Notes:

[50] - This study was terminated early

[51] - This study was terminated early

[52] - This study was terminated early

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline in short Form-36 (SF-36)

End point title	Mean change from baseline in short Form-36 (SF-36)

End point description:

First, precoded numeric values are recoded per the scoring key given in Table 1. Note that all items are scored so that a high score defines a more favorable health state. In addition, each item is scored on a 0 to 100 range so that the lowest and highest possible scores are 0 and 100, respectively. Scores represent the percentage of total possible score achieved. In step 2, items in the same scale are averaged together to create the 8 scale scores. Table 2 lists the items averaged together to create each scale. Items that are left blank(missing data) are not taken into account when calculating the scale scores. Hence, scale scores represent the average for all items in the scale that the respondent answered

End point type	Secondary

End point timeframe:

At baseline, week 4, week 8, week 12, and week 18

End point values	BMS-931699/lulizumab injection	BMS-986142 50 mg tablet (round) or 150 mg tablet (oval)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[53]	0[54]	0[55]	
Units: subjects				
arithmetic mean (standard deviation)				
Week 4|	()	()	()	
Week 8|	()	()	()	
Week 12|	()	()	()	
Week 18|	()	()	()	

Notes:

[53] - This study was terminated early

[54] - This study was terminated early

[55] - This study was terminated early

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline in female Sexual Function Index (FSFI)

End point title	Mean change from baseline in female Sexual Function Index (FSFI)

End point description:

The Female Sexual Function Index (FSFI), a 19-item questionnaire, has been developed as a brief, multidimensional self-report instrument for assessing the key dimensions of sexual function in women

End point type	Secondary

End point timeframe:

At baseline, week 4, week 8, week 12, and week 18

End point values	BMS-931699/lulizumab injection	BMS-986142 50 mg tablet (round) or 150 mg tablet (oval)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[56]	0[57]	0[58]	
Units: subjects				
arithmetic mean (standard deviation)				
Week 4|	()	()	()	
Week 8|	()	()	()	
Week 12|	()	()	()	
Week 18|	()	()	()	

Notes:

[56] - This study was terminated early

[57] - This study was terminated early

[58] - This study was terminated early

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline in work participation and activity impairment questionnaire (WPAI)

End point title	Mean change from baseline in work participation and activity impairment questionnaire (WPAI)

End point description:

Affords calculation of 4 scales to measure the impact of IBD on different domains of impairment in work or other activities: absenteeism, presenteeism (impairment at work), productivity loss (overall work impairment), activity impairment

End point type	Secondary

End point timeframe:

At baseline, week 4, week 8, week 12, and week 18

End point values	BMS-931699/lulizumab injection	BMS-986142 50 mg tablet (round) or 150 mg tablet (oval)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[59]	0[60]	0[61]	
Units: subjects				
arithmetic mean (standard deviation)				
Week 4|	()	()	()	
Week 8|	()	()	()	
Week 12|	()	()	()	
Week 18|	()	()	()	

Notes:

[59] - This study was terminated early

[60] - This study was terminated early

[61] - This study was terminated early

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to 18 weeks	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received subcutaneous (SC) injection of placebo matched to 12.5 milligram (mg) lulizumab (BMS-931699) weekly (QW) and oral tablets of placebo matched to 350 mg BMS-986142 once daily (QD) for 12 weeks.	
Reporting group title	BMS-986142 350 mg QD
Reporting group description:	
Subjects received oral tablets of 350 mg BMS-986142 QD and placebo matched to SC injection of 12.5 mg lulizumab (BMS-931699) QW for 12 weeks.	
Reporting group title	Lulizumab (BMS-931699) 12.5mg QW
Reporting group description:	
Subjects received SC injection of 12.5 mg lulizumab (BMS-931699) QW and oral tablets of placebo matched to 350 mg BMS-986142 QD for 12 weeks.	

Serious adverse events	Placebo	BMS-986142 350 mg QD	Lulizumab (BMS-931699) 12.5mg QW
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Placebo	BMS-986142 350 mg QD	Lulizumab (BMS-931699) 12.5mg QW
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 7 (28.57%)	4 / 6 (66.67%)	4 / 5 (80.00%)

Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Injection site haematoma			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Injection site reaction			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Sensation of foreign body			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Anticoagulation drug level above therapeutic			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Rhinitis allergic			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Blood pressure increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Stress fracture			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Gastrointestinal inflammation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0

Muscle spasms			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Urinary tract infection			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
Bronchitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Gastroenteritis viral			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Influenza			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Soft tissue infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Hypertriglyceridaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Hypokalaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Vitamin B12 deficiency			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 August 2016	Corrected name of the PatGDA to SubGDA, provided better description of PK analysis for HCQ, clarified several exclusion criteria, removed cryoglobulins, removed requirement to mask local ESR results, added several abbreviations, added references to appendices, corrected secondary outcome of salivary flow to salivary flow rate, corrected typographical & formatting errors in the Notes section of the Flow Chart/Time and Events Schedule (Table 5.1-2), align the pregnancy section of the protocol with requirements in the BMS informed consent form template, and added Appendices for ACR-EULAR Classification Criteria for Primary Sjögren's Syndrome, as well as for all rating scales and PROs
13 February 2017	Added preliminary information regarding two drug-drug interaction studies for BMS-986142 and clarified guidance around certain concomitant medications related to those studies, including removal of hormone-eluting intrauterine devices (IUDs) as an allowable method of highly-effective contraception, changed the duration of male contraception from 90 days to 35 days posttreatment completion, removed the 7 year limitation on the diagnosis of Sjögren's syndrome for study inclusion, clarified exclusion criteria regarding the severity of pSS complications, added guidance around the use of additional eye preparations during the study, clarified physical examination requirements, clarified the duration of post-study follow-up, clarified when BMS-986142 or matching placebo and hydroxychloroquine (if applicable) should be brought to the investigational site for administration, clarified that all routine safety labs should be performed after a 10 hour fast, removed the Day 29/Week 4 HCQ intensive PK assessment, clarified when a serum pregnancy test is needed, updated the reference information for the ACR-EULAR Classification Criteria for Primary Sjögren's Syndrome, to note that the paraffin wax method of stimulated salivary flow is the preferred method over moistened gauze, clarified the materials provided, clarified site processing instructions for optional biopsy samples, and corrected typographical errors

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported