Clinical trial results:
A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PROOF-OF-CONCEPT STUDY TO EVALUATE THE EFFICACY AND SAFETY OF UCB5857 OVER 12 WEEKS IN SUBJECTS WITH PRIMARY SJGREN'S SYNDROME

Summary

EudraCT number	2014-004523-51
Trial protocol	GB ES FR SE GR IT
Global end of trial date	27 September 2017

Results information

Result version number	v1 (current)
This version publication date	13 October 2018
First version publication date	13 October 2018

Trial information

Trial identification

Sponsor protocol code	SS0004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02610543
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UK Registered Branch of UCB Pharma SA
Sponsor organisation address	208 Bath Road, Slough, United Kingdom, SL1 3WE
Public contact	Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.com
Scientific contact	Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.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	03 May 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 September 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to evaluate the efficacy on overall disease activity and safety of UCB5857 added to current treatment relative to placebo in subjects with primary Sjögren's Syndrome (pSS).

Protection of trial subjects:

During the conduct of the study all subjects were closely monitored.

Background therapy:

Background therapy as permitted in the protocol.

Evidence for comparator:

Not applicable.

Actual start date of recruitment	28 October 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Spain: 8
Country: Number of subjects enrolled	United Kingdom: 9
Worldwide total number of subjects	27
EEA total number of subjects	27

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)	18
From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study started to enroll patients in October 2015 and concluded prematurely in September 2017.

Pre-assignment

Screening details:

The Participant Flow refers to the Full Analysis Set (FAS).

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	Investigator, Subject, Assessor, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received a daily dose of matching placebo for 12 weeks.

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

Dosage and administration details:

Subjects were administered capsules of matching placebo once daily, for a duration of 12 weeks.

Arm title	UCB5857

Arm description:

Participants received a daily dose of 45 mg UCB5857 for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	UCB5857
Investigational medicinal product code	UCB5857
Other name	Seletalisib
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects were administered capsules of the investigational medicinal product (IMP) at doses of 5, 10, and 30 milligrams (mg) adding up to a total dose of 45 mg, once daily, for a duration of 12 weeks.

Number of subjects in period 1	Placebo	UCB5857
Started	14	13
Completed	12	8
Not completed	2	5
Adverse event, non-fatal	1	5
Protocol deviation	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received a daily dose of matching placebo for 12 weeks.	
Reporting group title	UCB5857
Reporting group description:	
Participants received a daily dose of 45 mg UCB5857 for 12 weeks.	

Reporting group values	Placebo	UCB5857	Total
Number of subjects	14	13	27
Age categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	9	9	18
>=65 years	5	4	9
Age continuous Units: years			
arithmetic mean	60.2	52.2	
standard deviation	± 9.9	± 16.1	-
Gender categorical Units: Subjects			
Female	13	12	25
Male	1	1	2

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received a daily dose of matching placebo for 12 weeks.	
Reporting group title	UCB5857
Reporting group description:	
Participants received a daily dose of 45 mg UCB5857 for 12 weeks.	
Subject analysis set title	Placebo (SS)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants received a daily dose of matching placebo for 12 weeks.	
Subject analysis set title	UCB5857 (SS)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants received a daily dose of 45 mg UCB5857 for 12 weeks.	
Subject analysis set title	Placebo (FAS)
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants received a daily dose of matching placebo for 12 weeks.	
Subject analysis set title	UCB5857 (FAS)
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants received a daily dose of 45 mg UCB5857 for 12 weeks.	

Primary: Change from Baseline to Week 12 in the European League Against Rheumatism Sjögren's Syndrome Disease Activity Index (ESSDAI)

End point title	Change from Baseline to Week 12 in the European League Against Rheumatism Sjögren's Syndrome Disease Activity Index (ESSDAI)
End point description:	
The ESSDAI is a physician administered questionnaire containing 12 organ-specific domains designed to measure disease activity.	
End point type	Primary
End point timeframe:	
Week 12	

End point values	Placebo (FAS)	UCB5857 (FAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	13		
Units: scores on a scale				
least squares mean (standard error)				
scores on a scale	-2.8 (± 1.5)	-5.4 (± 1.7)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The difference presented is 'UCB5857 45 mg minus Placebo'.
Analysis performed on ESSDAI using mixed model for repeated measures (MMRM) analysis with covariates of treatment, visit, Baseline ESSDAI, and treatment by visit interaction.

Note: A negative change from baseline indicates improvement while a positive change from baseline indicates worsening.

Comparison groups	Placebo (FAS) v UCB5857 (FAS)
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.266
Method	MMRM
Parameter estimate	Difference in ESSDAI score
Point estimate	-2.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.3
upper limit	2.11

Secondary: Change from Baseline to Week 4 in the European League Against Rheumatism Sjögren's Syndrome Disease Activity Index (ESSDAI)

End point title	Change from Baseline to Week 4 in the European League Against Rheumatism Sjögren's Syndrome Disease Activity Index (ESSDAI)

End point description:

The ESSDAI is a physician administered questionnaire containing 12 organ-specific domains designed to measure disease activity.

End point type	Secondary

End point timeframe:

Week 4

End point values	Placebo (FAS)	UCB5857 (FAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	13		
Units: scores on a scale				
least squares mean (standard error)				
scores on a scale	-1.5 (± 1.2)	-5.0 (± 1.2)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The difference presented is 'UCB5857 45 mg minus Placebo'.
Analysis performed on ESSDAI using mixed model for repeated measures (MMRM) analysis with covariates of treatment, visit, Baseline ESSDAI, and treatment by visit interaction.

Note: A negative change from baseline indicates improvement while a positive change from baseline indicates worsening.

Comparison groups	Placebo (FAS) v UCB5857 (FAS)
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	superiority
Method	MMRM
Parameter estimate	Difference in ESSDAI score
Point estimate	-3.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.97
upper limit	-0.02

Secondary: Change from Baseline to Week 8 in the European League Against Rheumatism Sjögren's Syndrome Disease Activity Index (ESSDAI)

End point title	Change from Baseline to Week 8 in the European League Against Rheumatism Sjögren's Syndrome Disease Activity Index (ESSDAI)

End point description:

The ESSDAI is a physician administered questionnaire containing 12 organ-specific domains designed to measure disease activity.

End point type	Secondary

End point timeframe:

Week 8

End point values	Placebo (FAS)	UCB5857 (FAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	10		
Units: scores on a scale				
least squares mean (standard error)				
scores on a scale	-0.6 (± 1.7)	-4.7 (± 1.9)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The difference presented is 'UCB5857 45 mg minus Placebo'.
Analysis performed on ESSDAI using mixed model for repeated measures (MMRM) analysis with

covariates of treatment, visit, Baseline ESSDAI, and treatment by visit interaction.

Note: A negative change from baseline indicates improvement while a positive change from baseline indicates worsening.

Comparison groups	Placebo (FAS) v UCB5857 (FAS)
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
Method	MMRM
Parameter estimate	Difference in ESSDAI score
Point estimate	-4.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.3
upper limit	1.22

Secondary: Change from Baseline to Week 12 in the EULAR Sjögren's Syndrome Patient Response Index (ESSPRI)

End point title	Change from Baseline to Week 12 in the EULAR Sjögren's Syndrome Patient Response Index (ESSPRI)

End point description:

The ESSPRI is a patient completed questionnaire to assess subjective patient symptoms, which includes 3 domains (dryness, limb pain and fatigue).

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo (FAS)	UCB5857 (FAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	8		
Units: scores on a scale				
least squares mean (standard error)				
scores on a scale	-0.573 (± 0.555)	-2.125 (± 0.675)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The difference presented is 'UCB5857 45 mg minus Placebo'.
Analysis performed on ESSPRI using MMRM analysis with covariates of treatment, visit, Baseline ESSPRI, and treatment by visit interaction.

Note: A negative change from baseline indicates improvement while a positive change from baseline indicates worsening.

Comparison groups	Placebo (FAS) v UCB5857 (FAS)

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
Method	MMRM
Parameter estimate	Difference in ESSPRI score
Point estimate	-1.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.39
upper limit	0.28

Secondary: Change from Baseline to Week 4 in the EULAR Sjögren's Syndrome Patient Response Index (ESSPRI)

End point title	Change from Baseline to Week 4 in the EULAR Sjögren's Syndrome Patient Response Index (ESSPRI)

End point description:

The ESSPRI is a patient completed questionnaire to assess subjective patient symptoms, which includes 3 domains (dryness, limb pain and fatigue).

End point type	Secondary

End point timeframe:

Week 4

End point values	Placebo (FAS)	UCB5857 (FAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	12		
Units: scores on a scale				
least squares mean (standard error)				
scores on a scale	-1.376 (± 0.411)	-1.617 (± 0.460)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The difference presented is 'UCB5857 45 mg minus Placebo'.
Analysis performed on ESSPRI using MMRM analysis with covariates of treatment, visit, Baseline ESSPRI, and treatment by visit interaction.

Note: A negative change from baseline indicates improvement while a positive change from baseline indicates worsening.

Comparison groups	Placebo (FAS) v UCB5857 (FAS)

Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
Method	MMRM
Parameter estimate	Difference in ESSPRI score
Point estimate	-0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.53
upper limit	1.05

Secondary: Change from Baseline to Week 8 in the EULAR Sjögren's Syndrome Patient Response Index (ESSPRI)

End point title	Change from Baseline to Week 8 in the EULAR Sjögren's Syndrome Patient Response Index (ESSPRI)

End point description:

The ESSPRI is a patient completed questionnaire to assess subjective patient symptoms, which includes 3 domains (dryness, limb pain and fatigue).

End point type	Secondary

End point timeframe:

Week 8

End point values	Placebo (FAS)	UCB5857 (FAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	9		
Units: scores on a scale				
least squares mean (standard error)				
scores on a scale	-0.741 (± 0.439)	-1.922 (± 0.505)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The difference presented is 'UCB5857 45 mg minus Placebo'.
Analysis performed on ESSPRI using MMRM analysis with covariates of treatment, visit, Baseline ESSPRI, and treatment by visit interaction.

Note: A negative change from baseline indicates improvement while a positive change from baseline indicates worsening.

Comparison groups	Placebo (FAS) v UCB5857 (FAS)

Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
Method	MMRM
Parameter estimate	Difference in ESSPRI score
Point estimate	-1.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.58
upper limit	0.22

Secondary: Change from Baseline to Week 12 in the stimulated salivary flow

End point title	Change from Baseline to Week 12 in the stimulated salivary flow

End point description:

The stimulated salivary flow test evaluates the status of salivary glands and the production of saliva. Saliva is collected into a graduated container after gustatory provocation with a stimulant.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo (FAS)	UCB5857 (FAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	6		
Units: mL/min				
least squares mean (standard error)				
mL/min	-0.105 (± 0.081)	-0.084 (± 0.113)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The difference presented is 'UCB5857 45 mg minus Placebo'.
Analysis performed on Stimulated Salivary Flow Rate using MMRM analysis with covariates of treatment, visit, Baseline Stimulated Salivary Flow Rate, and treatment by visit interaction.

Note: A positive change from baseline indicates improvement while a negative change from baseline indicates worsening.

Comparison groups	Placebo (FAS) v UCB5857 (FAS)

Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority
Method	MMRM
Parameter estimate	Difference in Stimulated Salivary Flow
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.27
upper limit	0.31

Secondary: Change from Baseline to Week 4 in the stimulated salivary flow

End point title	Change from Baseline to Week 4 in the stimulated salivary flow

End point description:

The stimulated salivary flow test evaluates the status of salivary glands and the production of saliva. Saliva is collected into a graduated container after gustatory provocation with a stimulant.

End point type	Secondary

End point timeframe:

Week 4

End point values	Placebo (FAS)	UCB5857 (FAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	10		
Units: mL/min				
least squares mean (standard error)				
mL/min	-0.189 (± 0.081)	0.063 (± 0.093)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The difference presented is 'UCB5857 45 mg minus Placebo'.
Analysis performed on Stimulated Salivary Flow Rate using MMRM analysis with covariates of treatment, visit, Baseline Stimulated Salivary Flow Rate, and treatment by visit interaction.

Note: A positive change from baseline indicates improvement while a negative change from baseline indicates worsening.

Comparison groups	Placebo (FAS) v UCB5857 (FAS)

Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
Method	MMRM
Parameter estimate	Difference in Stimulated Salivary Flow
Point estimate	0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.51

Secondary: Change from Baseline to Week 8 in the stimulated salivary flow

End point title	Change from Baseline to Week 8 in the stimulated salivary flow

End point description:

The stimulated salivary flow test evaluates the status of salivary glands and the production of saliva. Saliva is collected into a graduated container after gustatory provocation with a stimulant.

End point type	Secondary

End point timeframe:

Week 8

End point values	Placebo (FAS)	UCB5857 (FAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	7		
Units: mL/min				
least squares mean (standard error)				
mL/min	-0.116 (± 0.096)	0.254 (± 0.126)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The difference presented is 'UCB5857 45 mg minus Placebo'.
Analysis performed on Stimulated Salivary Flow Rate using MMRM analysis with covariates of treatment, visit, Baseline Stimulated Salivary Flow Rate, and treatment by visit interaction.

Note: A positive change from baseline indicates improvement while a negative change from baseline indicates worsening.

Comparison groups	Placebo (FAS) v UCB5857 (FAS)

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
Method	MMRM
Parameter estimate	Difference in Stimulated Salivary Flow
Point estimate	0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.04
upper limit	0.7

Secondary: Change from Baseline to Week 12 in the unstimulated salivary flow

End point title	Change from Baseline to Week 12 in the unstimulated salivary flow

End point description:

The unstimulated salivary flow test evaluates the status of salivary glands and the production of saliva. Saliva is collected into a graduated container without gustatory provocation.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo (FAS)	UCB5857 (FAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	6		
Units: mL/min				
least squares mean (standard error)				
mL/min	-0.024 (± 0.021)	-0.042 (± 0.029)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The difference presented is 'UCB5857 45 mg minus Placebo'.
Analysis performed on Unstimulated Salivary Flow Rate using MMRM analysis with covariates of treatment, visit, Baseline Unstimulated Salivary Flow Rate, and treatment by visit interaction.

Note: A positive change from baseline indicates improvement while a negative change from baseline indicates worsening.

Comparison groups	Placebo (FAS) v UCB5857 (FAS)

Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority
Method	MMRM
Parameter estimate	Difference in Unstimulated Salivary Flow
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.06

Secondary: Change from Baseline to Week 4 in the unstimulated salivary flow

End point title	Change from Baseline to Week 4 in the unstimulated salivary flow

End point description:

The unstimulated salivary flow test evaluates the status of salivary glands and the production of saliva. Saliva is collected into a graduated container without gustatory provocation.

End point type	Secondary

End point timeframe:

Week 4

End point values	Placebo (FAS)	UCB5857 (FAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	10		
Units: mL/min				
least squares mean (standard error)				
mL/min	0.060 (± 0.049)	0.012 (± 0.059)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The difference presented is 'UCB5857 45 mg minus Placebo'.
Analysis performed on Unstimulated Salivary Flow Rate using MMRM analysis with covariates of treatment, visit, Baseline Unstimulated Salivary Flow Rate, and treatment by visit interaction.

Note: A positive change from baseline indicates improvement while a negative change from baseline indicates worsening.

Comparison groups	Placebo (FAS) v UCB5857 (FAS)

Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
Method	MMRM
Parameter estimate	Difference in Unstimulated Salivary Flow
Point estimate	-0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.21
upper limit	0.12

Secondary: Change from Baseline to Week 8 in the unstimulated salivary flow

End point title	Change from Baseline to Week 8 in the unstimulated salivary flow

End point description:

The unstimulated salivary flow test evaluates the status of salivary glands and the production of saliva. Saliva is collected into a graduated container without gustatory provocation.

End point type	Secondary

End point timeframe:

Week 8

End point values	Placebo (FAS)	UCB5857 (FAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	7		
Units: mL/min				
least squares mean (standard error)				
mL/min	0.013 (± 0.034)	0.011 (± 0.044)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The difference presented is 'UCB5857 45 mg minus Placebo'.
Analysis performed on Unstimulated Salivary Flow Rate using MMRM analysis with covariates of treatment, visit, Baseline Unstimulated Salivary Flow Rate, and treatment by visit interaction.

Note: A positive change from baseline indicates improvement while a negative change from baseline indicates worsening.

Comparison groups	Placebo (FAS) v UCB5857 (FAS)

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
Method	MMRM
Parameter estimate	Difference in Unstimuated Salivary Flow
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.12
upper limit	0.12

Secondary: Change in sum total tear secretion from Baseline to Week 12 measured by Schirmer´s I test (without anesthesia)

End point title	Change in sum total tear secretion from Baseline to Week 12 measured by Schirmer´s I test (without anesthesia)

End point description:

The Schirmer's test measures basic tear function. A 35 mm x 5 mm size paper strip is inserted into each eye for a period of 5 minutes to measure the production of tears.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo (FAS)	UCB5857 (FAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	8		
Units: mm				
least squares mean (standard error)				
mm	0.5 (± 2.6)	-0.9 (± 3.3)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The difference presented is 'UCB5857 45 mg minus Placebo'.
Analysis performed on Schirmer’s I Test Sum Score using ANCOVA with covariates of treatment and Baseline Schirmer’s I Test Sum Score.

Note: A positive change from baseline indicates improvement while a negative change from baseline indicates worsening.

Comparison groups	Placebo (FAS) v UCB5857 (FAS)

Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANCOVA
Parameter estimate	Difference in Schirmer´s I score
Point estimate	-1.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.35
upper limit	7.52

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline (Week 1) to Day 114 or 30 days after final dose, in case of early termination	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups	
Reporting group title	Placebo (SS)
Reporting group description:	
Participants received a daily dose of matching placebo for 12 weeks.	
Reporting group title	UCB5857 (SS)
Reporting group description:	
Participants received a daily dose of 45 mg UCB5857 for 12 weeks.	

Serious adverse events	Placebo (SS)	UCB5857 (SS)	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 14 (7.14%)	3 / 13 (23.08%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Chondrocalcinosis pyrophosphate			

subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myopathy			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo (SS)	UCB5857 (SS)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 14 (92.86%)	12 / 13 (92.31%)	
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Hypertension			
subjects affected / exposed	2 / 14 (14.29%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 14 (14.29%)	1 / 13 (7.69%)	
occurrences (all)	2	1	
Chest pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Contrast media allergy			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Drug hypersensitivity			

subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Menorrhagia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Insomnia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	2	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	2	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Hepatic enzyme increased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	2	
Neutrophil count decreased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
White blood cell count decreased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Blood creatine phosphokinase			

increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Post procedural contusion			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Post procedural swelling			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Procedural pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 14 (14.29%)	3 / 13 (23.08%)	
occurrences (all)	3	3	
Dizziness			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Dysgeusia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Sensory disturbance			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Presyncope			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Vertigo			

subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Tinnitus			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Tympanic membrane disorder			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Dry eye			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 14 (0.00%)	5 / 13 (38.46%)	
occurrences (all)	0	8	
Abdominal pain			
subjects affected / exposed	0 / 14 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	3	
Nausea			
subjects affected / exposed	1 / 14 (7.14%)	2 / 13 (15.38%)	
occurrences (all)	1	5	
Abdominal distension			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Colitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Constipation			
subjects affected / exposed	1 / 14 (7.14%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Vomiting			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	2	
Gastrooesophageal reflux disease			

subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Oral pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Tooth loss			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 14 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	4	
Dermatitis allergic			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Erythema multiforme			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Dermatitis contact			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Psoriasis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Eczema			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Purpura			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Lichen planus			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Rash maculo-papular			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	

Rash vesicular			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Skin exfoliation			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Skin hypertrophy			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 14 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	
Neck pain			
subjects affected / exposed	0 / 14 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	
Arthralgia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Costochondritis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Myalgia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Pain in extremity			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Sjögren's syndrome			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Fracture nonunion			

subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Muscle contracture			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Conjunctivitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Herpes zoster			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Respiratory tract infection			
subjects affected / exposed	1 / 14 (7.14%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Skin infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Tracheitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	2	
Upper respiratory tract infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	1 / 14 (7.14%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Gingivitis			
subjects affected / exposed	2 / 14 (14.29%)	0 / 13 (0.00%)	
occurrences (all)	2	0	

Pharyngotonsillitis subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	0 / 13 (0.00%) 0	
Metabolism and nutrition disorders Cell death subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	1 / 13 (7.69%) 1	
Decreased appetite subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	1 / 13 (7.69%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 August 2015	The rationale for this substantial amendment dated 17-Aug-2015 was to consolidate feedback from Competent Authorities in United Kingdom (UK), France, and Spain, resulting in a new core protocol. The country-specific amendments (France Protocol Amendment 0.1 and 0.2 and UK Protocol Amendment 0.2) were incorporated into Global Protocol Amendment 1. In addition, the Spanish Competent Authority recommended the inclusion of electrocardiogram (ECG) assessments within the study design; this was also implemented within Global Protocol Amendment 1.
04 March 2016	The protocol dated 04-Mar-2016 was amended to provide further information regarding prohibited P-glycoprotein substrate (PGP) inhibitors. Rather than specify "strong" inhibitors, all known inhibitors were excluded until further information was obtained regarding UCB5857's PGP substrate status. To facilitate identification of known PGP inhibitors, a sample, but nonexhaustive, list of PGP inhibitors was added as a table to the protocol. In addition, the definition of the Pharmacokinetic Set (PKS) was amended to correct an error. Previously the PK Set was incorrectly defined as a subset of the Full Analysis Set (FAS) when it should have been a subset of the Safety Set where subjects were assigned to the actual treatment received rather than their randomized treatment.
24 July 2016	The protocol dated 24-Jul-2016 was amended as an urgent safety measure to include potential drug-induced liver injury (PDILI)-related exclusion criteria, withdrawal criteria, and guidance for the management of such cases. Cases of elevated alanine aminotransferase (ALT) and aspartate aminotransferase (AST) had been observed in 3 subjects receiving UCB5857 in ongoing studies, including 2 subjects in SS0004, and 1 subject in APD001 (open-label study of UCB5857 in subjects with activated phosphoinositide 3 kinase [PI3K] delta syndrome). All available blinded clinical data for these cases were medically assessed and in addition, all available data from other subjects in these ongoing studies were reviewed to identify any other potential cases of interest, but no other clinically relevant elevations in aminotransferases or other hepatobiliary laboratory values were noted. UCB considered that from the currently available information, there was a possible causal association of UCB5857 with increased aminotransferases. Consequently, additional risk minimization and pharmacovigilance measures were implemented in the protocol in order to safeguard study subjects against any possible liver injury caused by UCB5857. Additionally, and unrelated to the main purpose of the amendment, further guidance was provided on suspected transmission of an infectious agent via a medicinal product in alignment with UCB's updated procedures.
05 April 2017	The rationale for this substantial protocol amendment dated 05-Apr-2017 was to modify the restriction regarding PGP inhibitors and remove the table of PGP inhibitors from the protocol based on newly available nonclinical data. In addition, procedures for assessment and management of Tuberculosis (TB) were added in order to comply with the UCB policy applied to all UCB-Sponsored studies (excluding noninterventional studies) that included subjects with immunological diseases, who were at increased risk of TB infection either associated with the investigational drug, underlying disease, concomitant treatments, or other medical or sociological factors. Updates to the interim analysis section were made to include text stating that an interim analysis for futility may be performed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
27 September 2017	After reviewing the feasibility and projected completion date, the Sponsor has made the decision to stop the study early. The interim analysis which was conducted per protocol indicated that the study was not futile and the safety profile of seletalisib has not changed.	-

Notes:

Limitations and caveats

None reported