



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 (\pm 0.439) | -1.922 (\pm 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 occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 13 (0.00%) 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 occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 13 (0.00%) 0 | |
| Injury, poisoning and procedural complications | | | |
| Post procedural contusion subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 13 (0.00%) 0 | |
| Post procedural swelling subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 13 (0.00%) 0 | |
| Procedural pain subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 13 (0.00%) 0 | |
| Cardiac disorders | | | |
| Palpitations subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 1 / 13 (7.69%) 1 | |
| Nervous system disorders | | | |
| Headache subjects affected / exposed occurrences (all) | 2 / 14 (14.29%) 3 | 3 / 13 (23.08%) 3 | |
| Dizziness subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 1 / 13 (7.69%) 1 | |
| Dysgeusia subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 1 / 13 (7.69%) 1 | |
| Sensory disturbance subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 13 (0.00%) 0 | |
| Presyncope subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 1 / 13 (7.69%) 1 | |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |

| | | | |
|---|---------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 1 / 13 (7.69%) 1 | |
| Tinnitus subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 13 (0.00%) 0 | |
| Tympanic membrane disorder subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 13 (0.00%) 0 | |
| Eye disorders Dry eye subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 13 (0.00%) 0 | |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 5 / 13 (38.46%) 8 | |
| Abdominal pain subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 2 / 13 (15.38%) 3 | |
| Nausea subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 2 / 13 (15.38%) 5 | |
| Abdominal distension subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 1 / 13 (7.69%) 1 | |
| Colitis subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 1 / 13 (7.69%) 1 | |
| Constipation subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 1 / 13 (7.69%) 1 | |
| Vomiting subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 1 / 13 (7.69%) 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 occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 13 (0.00%) 0 | |
| Skin exfoliation subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 13 (0.00%) 0 | |
| Skin hypertrophy subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 13 (0.00%) 0 | |
| Renal and urinary disorders Renal impairment subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 13 (0.00%) 0 | |
| Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 2 / 13 (15.38%) 2 | |
| Neck pain subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 2 / 13 (15.38%) 2 | |
| Arthralgia subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 1 / 13 (7.69%) 1 | |
| Costochondritis subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 1 / 13 (7.69%) 1 | |
| Myalgia subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 1 / 13 (7.69%) 1 | |
| Pain in extremity subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 1 / 13 (7.69%) 1 | |
| Sjögren's syndrome subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 1 / 13 (7.69%) 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 | 0 / 14 (0.00%) | 1 / 13 (7.69%) | |
| occurrences (all) | 0 | 1 | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 13 (7.69%) | |
| occurrences (all) | 0 | 1 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|----------------|--|
| 17 August 2015 | <p>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.</p> <p>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.</p> |
| 04 March 2016 | <p>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.</p> <p>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.</p> |
| 24 July 2016 | <p>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.</p> <p>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.</p> |
| 05 April 2017 | <p>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.</p> |

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