



Clinical trial results:

A Phase 3, Multi-center, Randomized, Double-Masked Study to Evaluate the Clinical Efficacy and Safety of SHP640 (PVP-Iodine 0.6% and Dexamethasone 0.1%) Ophthalmic Suspension Compared to PVP-Iodine and Placebo in the Treatment of Adenoviral Conjunctivitis

Summary

| | |
|--------------------------|----------------------------|
| EudraCT number | 2016-002439-14 |
| Trial protocol | DE EE HU GB ES PL AT FR IT |
| Global end of trial date | 13 May 2019 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 27 November 2019 |
| First version publication date | 27 November 2019 |

Trial information

Trial identification

| | |
|-----------------------|------------|
| Sponsor protocol code | SHP640-301 |
|-----------------------|------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02998541 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Shire |
| Sponsor organisation address | 300 Shire Way, Lexington, United States, MA 02421 |
| Public contact | Study Director, Shire, 1 8668425335, ClinicalTransparency@shire.com |
| Scientific contact | Study Director, Shire, 1 8668425335, ClinicalTransparency@shire.com |

Notes:

Paediatric regulatory details

| | |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMA-001936-PIP01-16 |
| 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? | Yes |

Notes:

Results analysis stage

| | |
|--|-------------|
| Analysis stage | Final |
| Date of interim/final analysis | 13 May 2019 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 13 May 2019 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the efficacy of SHP640 based on clinical resolution (defined as absence of bulbar conjunctival injection and watery conjunctival discharge) compared with placebo in the treatment of subjects with adenoviral conjunctivitis in the study eye at Visit 3 (Day 6).

Protection of trial subjects:

The study sponsor and any third party to whom aspects of the study management or monitoring have been delegated undertake their assigned roles for this study in compliance with all applicable industry regulations, ICH GCP Guideline E6 (R2) (2016), EU Directive 2001/20/EC and its updates, as well as all applicable national and local laws and regulations.

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 27 March 2017 |
| 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 | United States: 144 |
| Country: Number of subjects enrolled | United Kingdom: 2 |
| Country: Number of subjects enrolled | Australia: 2 |
| Country: Number of subjects enrolled | Austria: 3 |
| Country: Number of subjects enrolled | Canada: 3 |
| Country: Number of subjects enrolled | Estonia: 16 |
| Country: Number of subjects enrolled | France: 1 |
| Country: Number of subjects enrolled | Germany: 2 |
| Country: Number of subjects enrolled | India: 21 |
| Country: Number of subjects enrolled | Israel: 7 |
| Country: Number of subjects enrolled | South Africa: 4 |
| Country: Number of subjects enrolled | Spain: 14 |
| Worldwide total number of subjects | 219 |
| EEA total number of subjects | 38 |

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) | 10 |
| Adolescents (12-17 years) | 13 |
| Adults (18-64 years) | 196 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 97 sites in 15 countries between 27 March 2017 to 13 May 2019.

Pre-assignment

Screening details:

A total of 219 subjects were randomized and 196 completed the study. Among which 219 were included in intent-to-treat (ITT) population, 217 in safety population, 83 in modified intent-to-treat (mITT) population. Two subjects were included in ITT population but not in safety population.

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 |

Arms

| | |
|------------------------------|--------|
| Are arms mutually exclusive? | Yes |
| Arm title | SHP640 |

Arm description:

Subjects administered one drop of SHP640 (0.1 percent [%] dexamethasone and 0.6% PVP-I) ophthalmic suspension in each eye 4 times daily (QID) for 7 days.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | SHP640 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Eye drops |
| Routes of administration | Ocular use |

Dosage and administration details:

Subjects administered one drop of SHP640 (0.1 % dexamethasone and 0.6% PVP-I) ophthalmic suspension in each eye 4 times daily for 7 days.

| | |
|------------------|------------|
| Arm title | PVP-I 0.6% |
|------------------|------------|

Arm description:

Subjects administered one drop of 0.6% PVP-I ophthalmic solution in each eye QID for 7 days.

| | |
|--|-------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Povidone Iodine (PVP-I) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Eye drops |
| Routes of administration | Ocular use |

Dosage and administration details:

Subjects administered one drop of 0.6% PVP-I ophthalmic solution in each eye QID for 7 days.

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description:

Subjects administered one drop of placebo ophthalmic solution in each eye QID for 7 days.

| | |
|----------|---------|
| Arm type | Placebo |
|----------|---------|

| | |
|--|------------|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Eye drops |
| Routes of administration | Ocular use |

Dosage and administration details:

Subjects administered one drop of placebo ophthalmic solution in each eye QID for 7 days.

| Number of subjects in period 1 | SHP640 | PVP-I 0.6% | Placebo |
|---------------------------------------|--------|------------|---------|
| Started | 86 | 90 | 43 |
| Completed | 78 | 81 | 37 |
| Not completed | 8 | 9 | 6 |
| Consent withdrawn by subject | 3 | 1 | - |
| Physician decision | - | - | 3 |
| Adverse event, non-fatal | 4 | 5 | 1 |
| Withdrawal by Parent/Guardian | - | - | 1 |
| Lost to follow-up | - | 3 | 1 |
| Protocol deviation | 1 | - | - |

Baseline characteristics

Reporting groups

| | |
|---|------------|
| Reporting group title | SHP640 |
| Reporting group description: | |
| Subjects administered one drop of SHP640 (0.1 percent [%] dexamethasone and 0.6% PVP-I) ophthalmic suspension in each eye 4 times daily (QID) for 7 days. | |
| Reporting group title | PVP-I 0.6% |
| Reporting group description: | |
| Subjects administered one drop of 0.6% PVP-I ophthalmic solution in each eye QID for 7 days. | |
| Reporting group title | Placebo |
| Reporting group description: | |
| Subjects administered one drop of placebo ophthalmic solution in each eye QID for 7 days. | |

| Reporting group values | SHP640 | PVP-I 0.6% | Placebo |
|------------------------|--------|------------|---------|
| Number of subjects | 86 | 90 | 43 |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|---|---------|---------|---------|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 41.3 | 42.7 | 43.4 |
| standard deviation | ± 19.56 | ± 21.43 | ± 23.67 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 46 | 47 | 24 |
| Male | 40 | 43 | 19 |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 2 | 0 |
| Asian | 14 | 11 | 5 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 9 | 11 | 5 |
| White | 62 | 64 | 30 |
| More than one race | 0 | 0 | 3 |
| Unknown or Not Reported | 1 | 2 | 0 |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 23 | 16 | 10 |
| Not Hispanic or Latino | 63 | 73 | 31 |
| Unknown or Not Reported | 0 | 1 | 2 |

| Reporting group values | Total | | |
|------------------------|-------|--|--|
| Number of subjects | 219 | | |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|---|-----|--|--|
| Age continuous Units: years arithmetic mean standard deviation | - | | |
| Gender categorical Units: Subjects | | | |
| Female | 117 | | |
| Male | 102 | | |
| Race (NIH/OMB) Units: Subjects | | | |
| American Indian or Alaska Native | 2 | | |
| Asian | 30 | | |
| Native Hawaiian or Other Pacific Islander | 0 | | |
| Black or African American | 25 | | |
| White | 156 | | |
| More than one race | 3 | | |
| Unknown or Not Reported | 3 | | |
| Ethnicity (NIH/OMB) Units: Subjects | | | |
| Hispanic or Latino | 49 | | |
| Not Hispanic or Latino | 167 | | |
| Unknown or Not Reported | 3 | | |

End points

End points reporting groups

| | |
|---|------------|
| Reporting group title | SHP640 |
| Reporting group description: Subjects administered one drop of SHP640 (0.1 percent [%] dexamethasone and 0.6% PVP-I) ophthalmic suspension in each eye 4 times daily (QID) for 7 days. | |
| Reporting group title | PVP-I 0.6% |
| Reporting group description: Subjects administered one drop of 0.6% PVP-I ophthalmic solution in each eye QID for 7 days. | |
| Reporting group title | Placebo |
| Reporting group description: Subjects administered one drop of placebo ophthalmic solution in each eye QID for 7 days. | |

Primary: Number of Subjects With Clinical Resolution Among Who Received SHP640 or Placebo on Day 6

| | |
|--|--|
| End point title | Number of Subjects With Clinical Resolution Among Who Received SHP640 or Placebo on Day 6 ^[1] |
| End point description: Clinical resolution of adenoviral conjunctivitis was defined as the absence (score=0) of bulbar conjunctival injection and watery conjunctival discharge in the study eye. The study eye was defined based on subjects bulbar conjunctival redness and watery conjunctival discharge scores at baseline as well as his/her CC-IFA results at baseline. Bulbar conjunctival injection was assessed based on a 0 (Normal conjunctival vascular pattern)-4 (Markedly prominent, intense diffuse hyperemia) scale which used pictures from the validated bulbar redness (VBR) scale. Watery conjunctival discharge was assessed based on a 0-3 scale (0 – None and 3 - Severe: Abundant quantity of watery discharge observed in the lower conjunctival fornix and in the lower lid margin). Higher score represent worse symptoms for both scores. mITT population was analyzed. Here, the number of subjects analyzed refer to subjects evaluable for this endpoint at specific arm group. | |
| End point type | Primary |
| End point timeframe: Day 6 | |
| 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: The statistical analysis was not planned and not calculated. | |

| End point values | SHP640 | PVP-I 0.6% | Placebo | |
|-----------------------------|-----------------|------------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 32 | 0 ^[2] | 14 | |
| Units: Subjects | | | | |
| Subjects | 3 | | 1 | |

Notes:

[2] - No subject was analyzed for this reporting group in the endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinical Resolution Among Who Received SHP640 or Povidone-Iodine (PVP-I) on Day 6

| | |
|---|---|
| End point title | Number of Subjects With Clinical Resolution Among Who Received SHP640 or Povidone-Iodine (PVP-I) on Day 6 |
| End point description: | |
| Clinical resolution of adenoviral conjunctivitis was defined as the absence (score=0) of bulbar conjunctival injection and watery conjunctival discharge in the study eye. The study eye was defined based on subjects bulbar conjunctival redness and watery conjunctival discharge scores at baseline as well as his/her CC-IFA results at baseline. Bulbar conjunctival injection was assessed based on a 0 (Normal conjunctival vascular pattern)-4 (Markedly prominent, intense diffuse hyperemia) scale which used pictures from the validated bulbar redness (VBR) scale. Watery conjunctival discharge was assessed based on a 0-3 scale (0 – None and 3 - Severe: Abundant quantity of watery discharge observed in the lower conjunctival fornix and in the lower lid margin). Higher score represent worse symptoms for both scores. mITT population was analyzed. Here,the number of subjects analyzed refer to subjects evaluable for this endpoint at specific arm group. | |
| End point type | Secondary |
| End point timeframe: | |
| Day 6 | |

| End point values | SHP640 | PVP-I 0.6% | Placebo | |
|-----------------------------|-----------------|-----------------|------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 32 | 28 | 0 ^[3] | |
| Units: Subjects | | | | |
| Subjects | 3 | 1 | | |

Notes:

[3] - No subject was analyzed for this reporting group in the endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinical Resolution Among Who Received Povidone-Iodine (PVP-I) or Placebo on Day 6

| | |
|---|--|
| End point title | Number of Subjects With Clinical Resolution Among Who Received Povidone-Iodine (PVP-I) or Placebo on Day 6 |
| End point description: | |
| Clinical resolution of adenoviral conjunctivitis was defined as the absence (score=0) of bulbar conjunctival injection and watery conjunctival discharge in the study eye. The study eye was defined based on subjects bulbar conjunctival redness and watery conjunctival discharge scores at baseline as well as his/her CC-IFA results at baseline. Bulbar conjunctival injection was assessed based on a 0 (Normal conjunctival vascular pattern)-4 (Markedly prominent, intense diffuse hyperemia) scale which used pictures from the validated bulbar redness (VBR) scale. Watery conjunctival discharge was assessed based on a 0-3 scale (0 – None and 3 - Severe: Abundant quantity of watery discharge observed in the lower conjunctival fornix and in the lower lid margin). Higher score represent worse symptoms for both scores. mITT population was analyzed. Here,the number of subjects analyzed refer to subjects evaluable for this endpoint at specific arm group. | |
| End point type | Secondary |
| End point timeframe: | |
| Day 6 | |

| End point values | SHP640 | PVP-I 0.6% | Placebo | |
|-----------------------------|------------------|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[4] | 28 | 14 | |
| Units: Subjects | | | | |
| Subjects | | 1 | 1 | |

Notes:

[4] - No subject was analyzed for this reporting group in the endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Adenoviral Eradication Among Who Received Povidone-Iodine (PVP-I) or Placebo on Day 3

| | |
|-----------------|---|
| End point title | Number of Subjects With Adenoviral Eradication Among Who Received Povidone-Iodine (PVP-I) or Placebo on Day 3 |
|-----------------|---|

End point description:

Adenoviral eradication for the study eye was defined as negative Cell Culture- Immunofluorescence Assay (CC-IFA) in that eye. Positive CC-IFA is considered not reaching adenoviral eradication. CC-IFA for each eye was conducted using conjunctival swab samples collected at each visit to determine the presence of adenovirus. The study eye was defined based on subjects bulbar conjunctival redness and watery conjunctival discharge scores at baseline as well as his/her CC-IFA results at baseline. mITT population consisted of a subset of the ITT population (ITT population consisted of all screened subjects who were randomized) who received at least one dose of investigational product (IP) and had a positive CC-IFA adenovirus test at baseline in the study eye. Here, the number of subjects analyzed refer to the subjects evaluable for this endpoint at specific reporting arm.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 3

| End point values | SHP640 | PVP-I 0.6% | Placebo | |
|-----------------------------|------------------|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[5] | 27 | 15 | |
| Units: Subjects | | | | |
| Subjects | | 8 | 2 | |

Notes:

[5] - No subject was analyzed for this reporting group in the endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Adenoviral Eradication Among Who Received SHP640 or Placebo on Day 6

| | |
|-----------------|--|
| End point title | Number of Subjects With Adenoviral Eradication Among Who Received SHP640 or Placebo on Day 6 |
|-----------------|--|

End point description:

Adenoviral eradication for the study eye was defined as negative CC-IFA in that eye. CC-IFA for each eye was conducted using conjunctival swab samples collected at each visit to determine the presence of adenovirus. The study eye was defined based on subjects bulbar conjunctival redness and watery conjunctival discharge scores at baseline as well as his/her CC-IFA results at baseline. mITT population

consisted of a subset of the ITT population who received at least one dose of investigational product (IP) and had a positive CC-IFA adenovirus test at baseline in the study eye. Here, the number of subjects analyzed refer to the subjects evaluable for this endpoint at specific reporting arm.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Day 6 | |

| End point values | SHP640 | PVP-I 0.6% | Placebo | |
|-----------------------------|-----------------|------------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 30 | 0 ^[6] | 14 | |
| Units: Subjects | | | | |
| Subjects | 14 | | 7 | |

Notes:

[6] - No subject was analyzed for this reporting group in the endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Adenoviral Eradication Among Who Received SHP640 or Povidone-Iodine (PVP-I) on Day 6

| | |
|-----------------|--|
| End point title | Number of Subjects With Adenoviral Eradication Among Who Received SHP640 or Povidone-Iodine (PVP-I) on Day 6 |
|-----------------|--|

End point description:

Adenoviral eradication for the study eye was defined as negative CC-IFA in that eye. CC-IFA for each eye was conducted using conjunctival swab samples collected at each visit to determine the presence of adenovirus. The study eye was defined based on subjects bulbar conjunctival redness and watery conjunctival discharge scores at baseline as well as his/her CC-IFA results at baseline. mITT population consisted of a subset of the ITT population who received at least one dose of investigational product (IP) and had a positive CC-IFA adenovirus test at baseline in the study eye. Here, the number of subjects analyzed refer to the subjects evaluable for this endpoint at specific reporting arm.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Day 6 | |

| End point values | SHP640 | PVP-I 0.6% | Placebo | |
|-----------------------------|-----------------|-----------------|------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 30 | 28 | 0 ^[7] | |
| Units: Subjects | | | | |
| Subjects | 14 | 20 | | |

Notes:

[7] - No subject was analyzed for this reporting group in the endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Adenovirus Viral Titer as Assessed by Quantitative Polymerase Chain Reaction (qPCR) at Day 6 and 8

| | |
|-----------------|--|
| End point title | Percent Change From Baseline in Adenovirus Viral Titer as Assessed by Quantitative Polymerase Chain Reaction (qPCR) at Day 6 and 8 |
|-----------------|--|

End point description:

Percent change from baseline in adenovirus viral titer as assessed by qPCR was reported. The sponsor discontinued the SHP640 clinical development program and, thus, terminated this study. Hence, for this endpoint, the planned data collection and analysis was not performed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 6, 8

| End point values | SHP640 | PVP-I 0.6% | Placebo | |
|-----------------------------|------------------|------------------|-------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[8] | 0 ^[9] | 0 ^[10] | |
| Units: Subjects | | | | |

Notes:

[8] - The analysis was not performed due to study termination.

[9] - The analysis was not performed due to study termination.

[10] - The analysis was not performed due to study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Adenoviral Eradication on Day 8 and 12

| | |
|-----------------|--|
| End point title | Number of Subjects with Adenoviral Eradication on Day 8 and 12 |
|-----------------|--|

End point description:

Adenoviral eradication for the study eye was defined as negative CC-IFA in that eye. CC-IFA for each eye was conducted using conjunctival swab samples collected at each visit to determine the presence of adenovirus. The study eye was defined based on subjects bulbar conjunctival redness and watery conjunctival discharge scores at baseline as well as his/her CC-IFA results at baseline. mITT population consisted of a subset of the ITT population who received at least one dose of investigational product (IP) and had a positive CC-IFA adenovirus test at baseline in the study eye. Here, n = subjects evaluable for specified category for each arm, respectively. ET=Early Termination

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 8 and 12/ET

| End point values | SHP640 | PVP-I 0.6% | Placebo | |
|-----------------------------|-----------------|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 36 | 32 | 15 | |
| Units: Subjects | | | | |
| Day 8 (n=28, 28, 15) | 20 | 22 | 13 | |
| Day 12/ET (n= 31, 31, 14) | 28 | 28 | 13 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinical Resolution on Day 3, 8, 12

| | |
|-----------------|---|
| End point title | Number of Subjects With Clinical Resolution on Day 3, 8, 12 |
|-----------------|---|

End point description:

Clinical resolution of adenoviral conjunctivitis was defined as the absence (score=0) of bulbar conjunctival injection and watery conjunctival discharge in the study eye. The study eye was defined based on subjects bulbar conjunctival redness and watery conjunctival discharge scores at baseline as well as his/her CC-IFA results at baseline. Bulbar conjunctival injection was assessed based on a 0 (Normal conjunctival vascular pattern)-4 (Markedly prominent, intense diffuse hyperemia) scale which used pictures from the validated bulbar redness (VBR) scale. Watery conjunctival discharge was assessed based on a 0-3 scale (0 – None and 3 - Severe: Abundant quantity of watery discharge observed in the lower conjunctival fornix and in the lower lid margin). Higher score represent worse symptoms for both scores. mITT population was analyzed. Here, n = subjects evaluable for specified category for each arm, respectively. ET=Early Termination

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 3, 8, 12/ET

| End point values | SHP640 | PVP-I 0.6% | Placebo | |
|-----------------------------|-----------------|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 36 | 32 | 15 | |
| Units: Subjects | | | | |
| Day 3 (n=34, 30, 15) | 0 | 0 | 0 | |
| Day 8 (n=29, 28, 15) | 6 | 5 | 3 | |
| Day 12/ET (n=32, 31, 14) | 20 | 13 | 8 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Individual Clinical Signs Score at Day 3, 6, 8, 12

| | |
|-----------------|--|
| End point title | Change from Baseline in Individual Clinical Signs Score at Day 3, 6, 8, 12 |
|-----------------|--|

End point description:

The Individual clinical signs score (bulbar conjunctival injection and watery conjunctival discharge) in the study were reported. The study eye was defined based on subjects bulbar conjunctival redness and watery conjunctival discharge scores at baseline as well as his/her CC-IFA results at baseline. The sponsor discontinued the SHP640 clinical development program and, thus, terminated this study. Hence, for this endpoint, the planned data collection and analysis was not performed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 3, 6, 8, 12

| End point values | SHP640 | PVP-I 0.6% | Placebo | |
|-----------------------------|-------------------|-------------------|-------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[11] | 0 ^[12] | 0 ^[13] | |
| Units: Subjects | | | | |

Notes:

[11] - The analysis was not performed due to study termination.

[12] - The analysis was not performed due to study termination.

[13] - The analysis was not performed due to study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with at Least 2 Point Reduction From Baseline in the Global Clinical Score at Day 3, 6, 8 and 12

| | |
|-----------------|---|
| End point title | Number of Subjects with at Least 2 Point Reduction From Baseline in the Global Clinical Score at Day 3, 6, 8 and 12 |
|-----------------|---|

End point description:

Global clinical score was the sum of bulbar conjunctival injection and watery conjunctival discharge. The study eye was defined based on subjects bulbar conjunctival redness and watery conjunctival discharge scores at baseline as well as his/her CC-IFA results at baseline. mITT population consisted of a subset of the ITT population who received at least one dose of investigational product (IP) and had a positive CC-IFA adenovirus test at baseline in the study eye. Here, n = subjects evaluable for specified category for each arm, respectively. ET=Early Termination

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 3, 6, 8 and 12/ET

| End point values | SHP640 | PVP-I 0.6% | Placebo | |
|-----------------------------|-----------------|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 36 | 32 | 15 | |
| Units: Subjects | | | | |
| Day 3 (n=34, 30, 15) | 15 | 5 | 7 | |
| Day 6 (n=32,28,14) | 22 | 20 | 11 | |
| Day 8 (n=29, 28, 15) | 24 | 23 | 13 | |
| Day 12/ET (n=32, 31,14) | 30 | 27 | 12 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Modified Clinical Resolution on Day 3, 6, 8, 12

| | |
|---|---|
| End point title | Number of Subjects with Modified Clinical Resolution on Day 3, 6, 8, 12 |
| End point description: | |
| Modified clinical resolution was defined as a global clinical score of 0 or 1. Global clinical score was the sum of bulbar conjunctival injection and watery conjunctival discharge. The study eye was defined based on subjects bulbar conjunctival redness and watery conjunctival discharge scores at baseline as well as his/her CC-IFA results at baseline. The sponsor discontinued the SHP640 clinical development program and, thus, terminated this study. Hence, for this endpoint, the planned data collection and analysis was not performed. | |
| End point type | Secondary |
| End point timeframe: | |
| Day 3, 6, 8, 12 | |

| End point values | SHP640 | PVP-I 0.6% | Placebo | |
|-----------------------------|-------------------|-------------------|-------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[14] | 0 ^[15] | 0 ^[16] | |
| Units: Subjects | | | | |

Notes:

[14] - The analysis was not performed due to study termination.

[15] - The analysis was not performed due to study termination.

[16] - The analysis was not performed due to study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Expanded Clinical Resolution on Day 3, 6, 8, 12

| | |
|--|---|
| End point title | Number of Subjects with Expanded Clinical Resolution on Day 3, 6, 8, 12 |
| End point description: | |
| Expanded clinical resolution was defined as a global clinical score of 0, 1, or 2 with neither injection nor discharge having a score of 2. Global clinical score was the sum of bulbar conjunctival injection and watery conjunctival discharge. The study eye was defined based on subjects bulbar conjunctival redness and watery conjunctival discharge scores at baseline as well as his/her CC-IFA results at baseline. The sponsor discontinued the SHP640 clinical development program and, thus, terminated this study. Hence, for this endpoint, the planned data collection and analysis was not performed. | |
| End point type | Secondary |
| End point timeframe: | |
| Day 3, 6, 8, 12 | |

| End point values | SHP640 | PVP-I 0.6% | Placebo | |
|-----------------------------|-------------------|-------------------|-------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[17] | 0 ^[18] | 0 ^[19] | |
| Units: Subjects | | | | |

Notes:

[17] - The analysis was not performed due to study termination.

[18] - The analysis was not performed due to study termination.

[19] - The analysis was not performed due to study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Status of Cross-over Infection on Day 3, 6, 8, 12

| | |
|-----------------|---|
| End point title | Number of Subjects with Status of Cross-over Infection on Day 3, 6, 8, 12 |
|-----------------|---|

End point description:

Number of subjects with status of cross-over infection to a subject's fellow eye. Subjects with only 1 infected eye at baseline were reported. The sponsor discontinued the SHP640 clinical development program and, thus, terminated this study. Hence, for this endpoint, the planned data collection and analysis was not performed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 3, 6, 8, 12

| End point values | SHP640 | PVP-I 0.6% | Placebo | |
|-----------------------------|-------------------|-------------------|-------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[20] | 0 ^[21] | 0 ^[22] | |
| Units: Subjects | | | | |

Notes:

[20] - The analysis was not performed due to study termination.

[21] - The analysis was not performed due to study termination.

[22] - The analysis was not performed due to study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Clinical Resolution on Day 3, 6, 8, 12

| | |
|-----------------|--|
| End point title | Time to Clinical Resolution on Day 3, 6, 8, 12 |
|-----------------|--|

End point description:

Time to clinical resolution were reported based on the assessments in the study eye. The sponsor discontinued the SHP640 clinical development program and, thus, terminated this study. Hence, for this endpoint, the planned data collection and analysis was not performed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 3, 6, 8, 12

| End point values | SHP640 | PVP-I 0.6% | Placebo | |
|-------------------------------|-------------------|-------------------|-------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[23] | 0 ^[24] | 0 ^[25] | |
| Units: Hours | | | | |
| median (full range (min-max)) | (to) | (to) | (to) | |

Notes:

[23] - The analysis was not performed due to study termination.

[24] - The analysis was not performed due to study termination.

[25] - The analysis was not performed due to study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Treatment-Emergent Adverse Events (TEAEs) and Serious Adverse Event (SAEs) of SHP640

| | |
|-----------------|--|
| End point title | Number of Subjects with Treatment-Emergent Adverse Events (TEAEs) and Serious Adverse Event (SAEs) of SHP640 |
|-----------------|--|

End point description:

An Adverse Event (AE) was any untoward medical occurrence in a clinical investigation subject administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. A SAE was any untoward medical occurrence (whether considered to be related to investigational product or not) that at any dose: results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital abnormality/birth defect, is an important medical event. Any AE that occurred after the first dose of IP instillation was considered a TEAE. Safety Population consisted of all subjects who received at least one dose of investigational product (IP).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From start of the study up to Day 14

| End point values | SHP640 | PVP-I 0.6% | Placebo | |
|-------------------------------|-----------------|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 86 | 90 | 41 | |
| Units: Subjects | | | | |
| Number of subjects with TEAEs | 23 | 28 | 10 | |
| Number of subjects with SAEs | 0 | 1 | 0 | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of the study up to Day 14

Adverse event reporting additional description:

219 subjects were included in ITT population but only 217 subjects were included in safety population.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 19.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------|
| Reporting group title | SHP640 |
|-----------------------|--------|

Reporting group description:

Subjects administered one drop of SHP640 (0.1 percent [%] dexamethasone and 0.6% PVP-I) ophthalmic suspension in each eye 4 times daily (QID) for 7 days.

| | |
|-----------------------|------------|
| Reporting group title | PVP-I 0.6% |
|-----------------------|------------|

Reporting group description:

Subjects administered one drop of PVP-I ophthalmic solution in each eye QID (with a minimum of 2 hours between doses) for 7 days.

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Subjects administered one drop of placebo ophthalmic solution in each eye QID (with a minimum of 2 hours between doses) for 7 days.

| Serious adverse events | SHP640 | PVP-I 0.6% | Placebo |
|---|----------------|----------------|----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 90 (1.11%) | 0 / 41 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Infections and infestations | | | |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 90 (1.11%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 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 | SHP640 | PVP-I 0.6% | Placebo |
|---|------------------|----------------|----------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 12 / 86 (13.95%) | 8 / 90 (8.89%) | 1 / 41 (2.44%) |

| | | | |
|--|------------------|----------------|----------------|
| General disorders and administration site conditions | | | |
| Instillation site pain | | | |
| subjects affected / exposed | 12 / 86 (13.95%) | 8 / 90 (8.89%) | 1 / 41 (2.44%) |
| occurrences (all) | 12 | 8 | 1 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 30 June 2016 | -No subjects were enrolled under the original protocol, and Amendment 1 was the initial effective protocol for this study. |
| 28 November 2016 | -Added the discontinuation of subjects less than 2 months old who tested positive for the presence of chlamydia or gonorrhea. - Added the discontinuation of subjects who tested positive for Herpes simplex virus (HSV) in either eye at baseline and added testing for HSV by qPCR in all subjects at baseline. |
| 13 December 2017 | -Inclusion criterion stated that subjects must have had a clinical diagnosis of suspected adenoviral conjunctivitis in at least 1 eye. This must have been confirmed by the presence of minimal clinical signs and symptoms in that same eye. The window for one of these (presence of adenoviral conjunctivitis) was increased from less than or equal to (\leq) 3 days prior to Visit 1 to \leq 4 days prior to Visit 1. -Clarified the exclusion criterion relating to a clinical presentation more consistent with the diagnosis of non-infectious conjunctivitis. -Removed the exclusion criterion relating to subjects with a known history of elevated intraocular pressure greater than ($>$) 21 millimeters of mercury (mmHg). -Added windows for Study Visit 2, 4, and 5, and changed the window for the inclusion criterion relating to adenoviral conjunctivitis. -Clarified the safety follow-up to be conducted for subjects who tested positive for HSV in either eye. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was terminated as the clinical development of SHP640 was discontinued.

Notes: