



## 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
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##### 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:

<b>Subjects enrolled per age group</b>	
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
<b>Arm title</b>	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.

<b>Arm title</b>	PVP-I 0.6%
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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.

<b>Arm title</b>	Placebo
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Arm description:

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

Arm type	Placebo
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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.

<b>Number of subjects in period 1</b>	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 <sup>[1]</sup>
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 <sup>[2]</sup>	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 <sup>[3]</sup>	
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 <sup>[4]</sup>	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
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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
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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 <sup>[5]</sup>	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
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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 <sup>[6]</sup>	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
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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 <sup>[7]</sup>	
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
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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
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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 <sup>[8]</sup>	0 <sup>[9]</sup>	0 <sup>[10]</sup>	
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
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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
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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
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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
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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
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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
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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 <sup>[11]</sup>	0 <sup>[12]</sup>	0 <sup>[13]</sup>	
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
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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
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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 <sup>[14]</sup>	0 <sup>[15]</sup>	0 <sup>[16]</sup>	
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 <sup>[17]</sup>	0 <sup>[18]</sup>	0 <sup>[19]</sup>	
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
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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
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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 <sup>[20]</sup>	0 <sup>[21]</sup>	0 <sup>[22]</sup>	
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
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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
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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 <sup>[23]</sup>	0 <sup>[24]</sup>	0 <sup>[25]</sup>	
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
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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
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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
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.1
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### Reporting groups

Reporting group title	SHP640
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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%
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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
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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: