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 Placebo in the Treatment of Bacterial Conjunctivitis

Summary

EudraCT number	2016-003361-25
Trial protocol	DE EE HU ES PL AT FR GB IT
Global end of trial date	01 October 2018

Results information

Result version number	v1 (current)
This version publication date	10 April 2019
First version publication date	10 April 2019

Trial information

Trial identification

Sponsor protocol code	SHP640-303

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03004924
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, ClinicalTransparency@shire.com
Scientific contact	Study Director, Shire, ClinicalTransparency@shire.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-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	01 October 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 October 2018
Was the trial ended prematurely?	No

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 ocular conjunctival discharge) compared with placebo in the treatment of subjects with bacterial conjunctivitis in the study eye on Day 5.

Protection of trial subjects:

The study was conducted in accordance with applicable regulations, International Conference on Harmonisation (ICH), European Union (EU) Directive 2001/20/EC and its updates, and local ethical and legal requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 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	Australia: 9
Country: Number of subjects enrolled	Austria: 14
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Estonia: 21
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Hungary: 7
Country: Number of subjects enrolled	Israel: 14
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Poland: 2
Country: Number of subjects enrolled	Puerto Rico: 11
Country: Number of subjects enrolled	South Africa: 18
Country: Number of subjects enrolled	Spain: 11
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	United States: 640
Worldwide total number of subjects	753
EEA total number of subjects	60

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)	10
Children (2-11 years)	66
Adolescents (12-17 years)	27
Adults (18-64 years)	482
From 65 to 84 years	158
85 years and over	10

Subject disposition

Recruitment

Recruitment details:

Study was conducted at 121 centers in 14 countries between 29 Mar 2017 (first subject first visit) and 01 Oct 2018 (last subject last visit).

Pre-assignment

Screening details:

A total of 1080 subjects were screened, of them 753 were randomized to treatment. One subject was randomized in error and therefore captured only in the intent-to-treat (ITT) 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 1 drop of SHP640 (povidone-iodine [PVP-I] 0.6 percent [%] and Dexamethasone 0.1%) ophthalmic suspension in each eye 4 times a day (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 1 drop of SHP640 ophthalmic suspension in each eye QID.

Arm title	PVP-I 0.6%

Arm description:

Subjects administered 1 drop of PVP-I 0.6% ophthalmic solution in each eye QID for 7 days.

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

Dosage and administration details:

Subjects administered 1 drop of PVP-I 0.6% ophthalmic solution in each eye QID.

Arm title	Placebo

Arm description:

Subjects administered 1 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 1 drop of placebo ophthalmic solution in each eye QID.

Number of subjects in period 1	SHP640	PVP-I 0.6%	Placebo
Started	324	108	321
Completed	297	94	293
Not completed	27	14	28
Terminated by Sponsor	-	-	1
Missed Study Visit	-	-	2
Consent withdrawn by subject	5	3	5
Physician decision	1	-	1
Screen Failure	1	-	-
Adverse event, non-fatal	6	5	10
HSV1 Positive	1	-	-
Pregnancy	-	1	-
Lost to follow-up	6	1	4
Withdrawal by parent/guardian	1	-	2
Protocol deviation	4	-	1
Lack of efficacy	2	4	2

Baseline characteristics

Reporting groups	
Reporting group title	SHP640
Reporting group description:	
Subjects administered 1 drop of SHP640 (povidone-iodine [PVP-I] 0.6 percent [%] and Dexamethasone 0.1%) ophthalmic suspension in each eye 4 times a day (QID) for 7 days.	
Reporting group title	PVP-I 0.6%
Reporting group description:	
Subjects administered 1 drop of PVP-I 0.6% ophthalmic solution in each eye QID for 7 days.	
Reporting group title	Placebo
Reporting group description:	
Subjects administered 1 drop of placebo ophthalmic solution in each eye QID for 7 days.	

Reporting group values	SHP640	PVP-I 0.6%	Placebo
Number of subjects	324	108	321
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	44.2	43.1	44.7
standard deviation	± 22.87	± 23.03	± 23.00
Gender categorical Units: Subjects			
Female	191	71	199
Male	133	37	122
Race/Ethnicity, Customized Units: Subjects			
Ethnicity Hispanic or Latino	62	30	87
Ethnicity Not Hispanic or Latino	254	76	230
Ethnicity Not reported	4	2	2
Ethnicity Other	4	0	2
Race/Ethnicity, Customized Units: Subjects			
Race American Indian or Alaska Native	0	1	3
Race Asian	12	0	8
Race Black or African American	54	18	54
Race White	250	88	250
Race Native Hawaiian or Other Pacific Islander	0	0	2
Race Other	6	1	4
Race Multiple	2	0	0

Reporting group values	Total		
Number of subjects	753		

Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	- 		
Gender categorical Units: Subjects			
Female	461		
Male	292		
Race/Ethnicity, Customized Units: Subjects			
Ethnicity Hispanic or Latino	179		
Ethnicity Not Hispanic or Latino	560		
Ethnicity Not reported	8		
Ethnicity Other	6		
Race/Ethnicity, Customized Units: Subjects			
Race American Indian or Alaska Native	4		
Race Asian	20		
Race Black or African American	126		
Race White	588		
Race Native Hawaiian or Other Pacific Islander	2		
Race Other	11		
Race Multiple	2		

End points

End points reporting groups

Reporting group title	SHP640
Reporting group description:	
Subjects administered 1 drop of SHP640 (povidone-iodine [PVP-I] 0.6 percent [%] and Dexamethasone 0.1%) ophthalmic suspension in each eye 4 times a day (QID) for 7 days.	
Reporting group title	PVP-I 0.6%
Reporting group description:	
Subjects administered 1 drop of PVP-I 0.6% ophthalmic solution in each eye QID for 7 days.	
Reporting group title	Placebo
Reporting group description:	
Subjects administered 1 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 5

End point title	Number of Subjects With Clinical Resolution Among who Received SHP640 or Placebo on Day 5[1]
End point description:	
Clinical resolution was defined as absence (score=0) of bulbar conjunctival injection and ocular conjunctival discharge in the study eye. Bulbar conjunctival injection was assessed based on 0 (Normal conjunctival vascular pattern)-4(Markedly prominent, intense diffuse hyperemia) scale which used pictures from validated bulbar redness (VBR) scale. Ocular conjunctival discharge was assessed based on 0 (No evidence of discharge in conjunctiva)-3 (Abundant quantity of mucopurulent or purulent discharge) scale. Study eye was defined as an eye with a score of at least 1 for both ocular conjunctival discharge and bulbar conjunctival redness at baseline. Modified intent-to-treat (mITT) population included subjects who received at least one dose of investigational product and had a positive bacterial culture (presence of one or more bacterial species at or above pathological threshold) at baseline. Here, number of subjects analyzed refer to evaluable subjects at specified time points.	
End point type	Primary
End point timeframe:	
Day 5	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to compare the efficacy between the SHP640 and placebo groups.

End point values	SHP640	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	220	222		
Units: Subjects				
Subjects	111	95		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v SHP640

Number of subjects included in analysis	442
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.127
Method	Fisher exact
Parameter estimate	Difference in response rate
Point estimate	7.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	16.9

Secondary: Number of Subjects With Bacterial Eradication Among who Received SHP640 or Placebo on Day 5

End point title	Number of Subjects With Bacterial Eradication Among who Received SHP640 or Placebo on Day 5[2]

End point description:

Bacterial eradication was defined as absence of all bacterial species present at or above pathological threshold at baseline in the study eye. Bacterial species were identified by Matrix Assisted Laser Desorption/Ionization-Time of Flight Mass Spectrometry, using their unique protein patterns. Pathological threshold for individual bacterial species was based on colony-forming unit (CFU)/mL threshold levels established by Cagle and modified by Leibowitz for different ocular bacterial species found in the specimens collected from each subject. mITT population included subjects who received at least one dose of IP and had a positive bacterial culture (presence of one or more bacterial species at or above pathological threshold) at baseline in the study. Here, the number of subjects analyzed refer to the subjects evaluable for this outcome at specified time point.

End point type	Secondary

End point timeframe:

Baseline, Day 5

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to compare the efficacy between the SHP640 and placebo groups.

End point values	SHP640	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	217	218		
Units: Subjects				
Subjects	94	102		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v SHP640

Number of subjects included in analysis	435
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5
Method	Fisher exact
Parameter estimate	Difference in response rate
Point estimate	-3.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.8
upper limit	5.9

Secondary: Number of Subjects With Clinical Resolution

End point title	Number of Subjects With Clinical Resolution

End point description:

Clinical resolution was defined as absence (score=0) of bulbar conjunctival injection and ocular conjunctival discharge in the study eye. Bulbar conjunctival injection was assessed based on 0 (Normal conjunctival vascular pattern) - 4(Markedly prominent, intense diffuse hyperemia) scale which used pictures from VBR scale. Ocular conjunctival discharge was assessed based on 0 (No evidence of discharge in conjunctiva)-3 (Abundant quantity of mucopurulent or purulent discharge) scale. Study eye was defined as an eye with a score of at least 1 for both ocular conjunctival discharge and bulbar conjunctival redness at baseline. mITT population included subjects who received at least one dose of investigational product and had a positive bacterial culture (presence of one or more bacterial species at or above pathological threshold) at baseline. in the study. Here, "n" refer to the subjects evaluable for this outcome at specified time point.

End point type	Secondary

End point timeframe:

Day 3, 8 and 12

End point values	SHP640	PVP-I 0.6%	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	223	76	227	
Units: Subjects				
Day 3 (n=215,76,218)	39	6	39	
Day 8 (n=205,65,206)	148	39	133	
Day 12 (n=195,62,187)	150	47	154	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Bacterial Eradication

End point title	Number of Subjects With Bacterial Eradication

End point description:

Bacterial eradication was defined as absence of all bacterial species present at or above pathological

threshold at baseline in the study eye. Bacterial species were identified by Matrix Assisted Laser Desorption/Ionization-Time of Flight Mass Spectrometry, using their unique protein patterns. Pathological threshold for individual bacterial species was based on CFU/mL threshold levels established by Cagle and modified by Leibowitz for different ocular bacterial species found in the specimens collected from each subject. mITT population included subjects who received at least one dose of IP and had a positive bacterial culture (presence of one or more bacterial species at or above pathological threshold) at baseline in the study. Here, "n" refer to the subjects evaluable for this outcome at specified time point.

End point type	Secondary

End point timeframe:

Day 3, 8 and 12

End point values	SHP640	PVP-I 0.6%	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	223	76	227	
Units: Subjects				
Day 3 (n=213,75,214)	76	33	79	
Day 8 (n=205,64,200)	85	25	87	
Day 12 (n=194,60,183)	83	21	82	

Statistical analyses

No statistical analyses for this end point

Secondary: Bulbar Conjunctival Injection Score

End point title	Bulbar Conjunctival Injection Score

End point description:

Bulbar conjunctival injection was assessed based on 0 (Normal conjunctival vascular pattern) - 4 (Markedly prominent, intense diffuse hyperemia) scale which used pictures from VBR scale. mITT population included subjects who received at least one dose of IP and had a positive bacterial culture (presence of one or more bacterial species at or above pathological threshold) at baseline in the study. Here, "n" refer to the subjects evaluable for this outcome at specified time point.

End point type	Secondary

End point timeframe:

Day 3, 5, 8 and 12

End point values	SHP640	PVP-I 0.6%	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	223	76	227	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Day 3 (n=216,76,218)	1.0 (± 0.84)	1.3 (± 0.90)	1.1 (± 0.86)	
Day 5 (n=207,65,209)	0.5 (± 0.77)	0.7 (± 0.88)	0.7 (± 0.80)	
Day 8 (n=205,65,206)	0.3 (± 0.64)	0.4 (± 0.61)	0.4 (± 0.61)	
Day 12 (n=196,62,187)	0.2 (± 0.56)	0.2 (± 0.47)	0.2 (± 0.48)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Bulbar Conjunctival Injection Score

End point title	Change From Baseline in the Bulbar Conjunctival Injection Score

End point description:

Bulbar conjunctival injection was assessed based on 0 (Normal conjunctival vascular pattern) - 4 (Markedly prominent, intense diffuse hyperemia) scale which used pictures from VBR scale. mITT population included subjects who received at least one dose of IP and had a positive bacterial culture (presence of one or more bacterial species at or above pathological threshold) at baseline in the study. Here, "n" refer to the subjects evaluable for this outcome at specified time point.

End point type	Secondary

End point timeframe:

Baseline, Day 3, 5, 8 and 12

End point values	SHP640	PVP-I 0.6%	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	223	76	227	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Day 3 (n=216,76,218)	-1.0 (± 0.77)	-0.8 (± 0.76)	-0.9 (± 0.76)	
Day 5 (n=207,65,209)	-1.5 (± 0.87)	-1.3 (± 0.99)	-1.3 (± 0.85)	
Day 8 (n=205,65,206)	-1.8 (± 0.91)	-1.6 (± 0.86)	-1.6 (± 0.81)	
Day 12 (n=196,62,187)	-1.8 (± 0.89)	-1.8 (± 0.74)	-1.8 (± 0.82)	

Statistical analyses

No statistical analyses for this end point

Secondary: Ocular Conjunctival Discharge Score

End point title	Ocular Conjunctival Discharge Score

End point description:

Ocular conjunctival discharge was assessed based on a 0 (No evidence of discharge in the conjunctiva) - 3 (Abundant quantity of mucopurulent or purulent discharge) scale. mITT population included subjects who received at least one dose of IP and had a positive bacterial culture (presence of one or more bacterial species at or above pathological threshold) at baseline in the study. Here, "n" refer to the subjects evaluable for this outcome at specified time point.

End point type	Secondary

End point timeframe:

Day 3, 5, 8 and 12

End point values	SHP640	PVP-I 0.6%	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	223	76	227	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Day 3 (n=215,76,218)	0.7 (± 0.73)	0.8 (± 0.74)	0.7 (± 0.76)	
Day 5 (n=206,65,209)	0.3 (± 0.57)	0.2 (± 0.44)	0.4 (± 0.60)	
Day 8 (n=205,65,206)	0.1 (± 0.43)	0.1 (± 0.31)	0.2 (± 0.47)	
Day 12 (n=195,62,187)	0.1 (± 0.49)	0.0 (± 0.22)	0.1 (± 0.28)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Ocular Conjunctival Discharge Score

End point title	Change From Baseline in the Ocular Conjunctival Discharge Score

End point description:

Ocular conjunctival discharge was assessed based on a 0 (No evidence of discharge in the conjunctiva) - 3 (Abundant quantity of mucopurulent or purulent discharge) scale. mITT population included subjects who received at least one dose of IP and had a positive bacterial culture (presence of one or more bacterial species at or above pathological threshold) at baseline in the study. Here, "n" refer to the subjects evaluable for this outcome at specified time point.

End point type	Secondary

End point timeframe:

Baseline, Day 3, 5, 8 and 12

End point values	SHP640	PVP-I 0.6%	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	223	76	227	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Day 3 (n=215,76,218)	-0.9 (± 0.77)	-0.8 (± 0.67)	-0.9 (± 0.85)	
Day 5 (n=206,65,209)	-1.4 (± 0.74)	-1.4 (± 0.75)	-1.3 (± 0.75)	
Day 8 (n=205,65,206)	-1.5 (± 0.71)	-1.5 (± 0.73)	-1.4 (± 0.74)	
Day 12 (n=195,62,187)	-1.5 (± 0.76)	-1.6 (± 0.71)	-1.6 (± 0.73)	

Statistical analyses

No statistical analyses for this end point

Secondary: Global Clinical Score

End point title	Global Clinical Score

End point description:

Global clinical score was defined as the sum of bulbar conjunctival injection and ocular conjunctival discharge scores. Bulbar conjunctival injection was assessed based on 0 (Normal conjunctival vascular pattern) - 4 (Markedly prominent, intense diffuse hyperemia) scale which used pictures from VBR scale. Ocular conjunctival discharge was assessed based on 0 (No evidence of discharge in conjunctiva) - 3 (Abundant quantity of mucopurulent or purulent discharge) scale. Study eye was defined as an eye with a score of at least 1 for both ocular conjunctival discharge and bulbar conjunctival redness at baseline. mITT population included subjects who received at least one dose of IP and had a positive bacterial culture (presence of one or more bacterial species at or above pathological threshold) at baseline in the study. Here, "n" refer to the subjects evaluable for this outcome at specified time point.

End point type	Secondary

End point timeframe:

Day 3, 5, 8 and 12

End point values	SHP640	PVP-I 0.6%	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	223	76	227	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Day 3 (n=215,76,218)	1.7 (± 1.37)	2.1 (± 1.39)	1.9 (± 1.42)	
Day 5 (n=206,65,209)	0.8 (± 1.18)	0.9 (± 1.19)	1.0 (± 1.18)	
Day 8 (n=205,65,206)	0.4 (± 0.93)	0.5 (± 0.77)	0.6 (± 0.93)	
Day 12 (n=195,62,187)	0.4 (± 0.90)	0.3 (± 0.55)	0.3 (± 0.67)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Global Clinical Score

End point title	Change From Baseline in the Global Clinical Score

End point description:

Global clinical score was defined as the sum of bulbar conjunctival injection and ocular conjunctival discharge scores. Bulbar conjunctival injection was assessed based on 0 (Normal conjunctival vascular pattern) - 4 (Markedly prominent, intense diffuse hyperemia) scale which used pictures from VBR scale. Ocular conjunctival discharge was assessed based on 0 (No evidence of discharge in conjunctiva) - 3 (Abundant quantity of mucopurulent or purulent discharge) scale. Study eye was defined as an eye with a score of at least 1 for both ocular conjunctival discharge and bulbar conjunctival redness at baseline. mITT population included subjects who received at least one dose of IP and had a positive bacterial culture (presence of one or more bacterial species at or above pathological threshold) at baseline in the study. Here, "n" refer to the subjects evaluable for this outcome at specified time point.

End point type	Secondary

End point timeframe:

Baseline, Day 3, 5, 8 and 12

End point values	SHP640	PVP-I 0.6%	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	223	76	227	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Day 3 (n=215,76,218)	-1.9 (± 1.28)	-1.6 (± 1.22)	-1.8 (± 1.30)	
Day 5 (n=206,65,209)	-2.9 (± 1.27)	-2.8 (± 1.47)	-2.6 (± 1.31)	
Day 8 (n=205,65,206)	-3.2 (± 1.36)	-3.2 (± 1.25)	-3.1 (± 1.25)	
Day 12 (n=195,62,187)	-3.3 (± 1.38)	-3.4 (± 1.06)	-3.3 (± 1.23)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Modified Clinical Resolution

End point title	Number of Subjects With Modified Clinical Resolution

End point description:

Modified clinical resolution was defined as a global clinical score of 0 or 1. Global clinical score was defined as the sum of bulbar conjunctival injection and ocular conjunctival discharge scores. Global clinical score was defined as the sum of bulbar conjunctival injection and ocular conjunctival discharge scores. Bulbar conjunctival injection was assessed based on 0 (Normal conjunctival vascular pattern) - 4 (Markedly prominent, intense diffuse hyperemia) scale which used pictures from VBR scale. Ocular conjunctival discharge was assessed based on 0 (No evidence of discharge in conjunctiva) - 3 (Abundant quantity of mucopurulent or purulent discharge) scale. mITT population included subjects who received at least one dose of IP and had a positive bacterial culture (presence of one or more bacterial species at or above pathological threshold) at baseline in the study. Here, "n" refer to the subjects evaluable for this outcome at specified time point.

End point type	Secondary

End point timeframe:

Day 3, 5, 8 and 12

End point values	SHP640	PVP-I 0.6%	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	223	76	227	
Units: Subjects				
Day 3 (n=215,76,218)	100	28	93	
Day 5 (n=206,65,209)	166	48	143	
Day 8 (n=205,65,206)	189	59	175	
Day 12 (n=195,62,187)	182	59	173	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Expanded Clinical Resolution

End point title	Number of Subjects With Expanded Clinical Resolution

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 defined as the sum of bulbar conjunctival injection and ocular conjunctival discharge scores. Bulbar conjunctival injection was assessed based on 0 (Normal conjunctival vascular pattern) - 4 (Markedly prominent, intense diffuse hyperemia) scale which used pictures from VBR scale. Ocular conjunctival discharge was assessed based on 0 (No evidence of discharge in conjunctiva) - 3 (Abundant quantity of mucopurulent or purulent discharge) scale. mITT population included subjects who received at least one dose of IP and had a positive bacterial culture (presence of one or more bacterial species at or above pathological threshold) at baseline in the study. Here, "n" refer to the subjects evaluable for this outcome at specified time point.

End point type	Secondary

End point timeframe:

Day 3, 5, 8 and 12

End point values	SHP640	PVP-I 0.6%	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	226	76	227	
Units: Subjects				
Day 3 (n=215,76,218)	155	46	154	
Day 5 (n=206,65,209)	185	54	171	
Day 8 (n=205,65,206)	193	63	192	
Day 12 (n=195,62,187)	185	61	181	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Clinical Resolution

End point title	Time to Clinical Resolution

End point description:

Clinical resolution was defined as absence (score of 0) of bulbar conjunctival injection and ocular conjunctival discharge in the study eye. Bulbar conjunctival injection was assessed based on 0 (Normal conjunctival vascular pattern) - 4 (Markedly prominent, intense diffuse hyperemia) scale which used pictures from VBR scale. Ocular conjunctival discharge was assessed based on 0 (No evidence of discharge in conjunctiva) - 3 (Abundant quantity of mucopurulent or purulent discharge) scale. Time to clinical resolution defined as the date on which a subject first reached clinical resolution minus the date of first dose of investigational product, plus 1. mITT population included subjects who received at least one dose of IP and had a positive bacterial culture (presence of one or more bacterial species at or above pathological threshold) at baseline in the study.

End point type	Secondary

End point timeframe:

Baseline to Day 12

End point values	SHP640	PVP-I 0.6%	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	223	76	227	
Units: Days				
median (confidence interval 95%)				
Days	5 (5.0 to 8.0)	6 (5.0 to 8.0)	8 (5.0 to 8.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects who Used Rescue Medication

End point title	Number of Subjects who Used Rescue Medication

End point description:

Rescue treatment with a licensed antibiotic according to the local standard of care was provided to participants if, in the judgment of the investigator, there was no clinical improvement or worsening of their condition to an extent that it would be in the best interest of the participant treated with an alternate therapy for safety reasons. mITT population included subjects who received at least one dose of IP and had a positive bacterial culture (presence of one or more bacterial species at or above pathological threshold) at baseline in the study.

End point type	Secondary

End point timeframe:

Baseline to Day 12

End point values	SHP640	PVP-I 0.6%	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	223	76	227	
Units: Subjects				
Subjects	2	3	4	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Treatment-emergent Adverse Events (TEAEs)

End point title	Number of Subjects with Treatment-emergent Adverse Events (TEAEs)

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. Any AE that occured after the first dose of investigational product instillation was considered a TEAE. Safety population included all subjects who received at least one dose of investigational product.

End point type	Secondary

End point timeframe:

From start of study drug administration up to 14 days

End point values	SHP640	PVP-I 0.6%	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	323	108	321	
Units: Subjects				
Subjects	106	43	61	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From start of study drug administration up to 14 days	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.1
Reporting groups	
Reporting group title	SHP640
Reporting group description:	
Subjects administered 1 drop of SHP640 ophthalmic suspension in each eye QID for 7 days.	
Reporting group title	Placebo
Reporting group description:	
Subjects administered 1 drop of placebo ophthalmic solution in each eye QID for 7 days.	
Reporting group title	PVP-I 0.6%
Reporting group description:	
Subjects administered 1 drop of PVP-I 0.6% ophthalmic solution in each eye QID for 7 days.	

Serious adverse events	SHP640	Placebo	PVP-I 0.6%
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 323 (0.00%)	0 / 321 (0.00%)	0 / 108 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	SHP640	Placebo	PVP-I 0.6%
Total subjects affected by non-serious adverse events			
subjects affected / exposed	67 / 323 (20.74%)	7 / 321 (2.18%)	26 / 108 (24.07%)
General disorders and administration site conditions			
Instillation site pain			
subjects affected / exposed	67 / 323 (20.74%)	7 / 321 (2.18%)	26 / 108 (24.07%)
occurrences (all)	68	7	26

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 November 2016	Aligned clinical strategy and language across the SHP640 adenoviral and bacterial conjunctivitis programs and updated the assessments and inclusion and exclusion criteria.
15 February 2017	- Added the Middle East and Africa to the list of regions participating in the study. - 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 HSV in either eye at baseline and added testing for HSV by qPCR in all subjects at baseline.
13 December 2017	- Added windows for Study Visit 2, 4, and 5, and changed the window for the inclusion criterion relating to bacterial conjunctivitis. - 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 >21 mmHg. - Clarified the safety follow up to be conducted for subjects who tested positive for HSV in either eye.
31 July 2018	- Increased the planned number of subjects to be randomized and the number of study sites, to ensure the target number of subjects in the mITT population would be achieved.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported