Clinical trial results:
A Phase 2a, Randomized, Double-blind, Placebo-controlled, Parallel-group, Proof of Concept Study to Investigate Efficacy, Safety, Pharmacodynamics and Pharmacokinetics of ASP6294 in the Treatment of Female Subjects With Bladder Pain Syndrome/Interstitial Cystitis

Summary

EudraCT number	2016-004138-12
Trial protocol	DE HU CZ GB BE PL NL LV ES
Global end of trial date	21 March 2019

Results information

Result version number	v1 (current)
This version publication date	08 February 2020
First version publication date	08 February 2020

Trial information

Trial identification

Sponsor protocol code	6294-CL-0101

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03282318
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Astellas Pharma Europe B.V.
Sponsor organisation address	Sylviusweg 62, Leiden, Netherlands, 2333 BE
Public contact	Astellas Pharma Global Development, Inc., Clinical Trial Disclosure, astellas.resultsdisclosure@astellas.com
Scientific contact	Astellas Pharma Global Development, Inc., Clinical Trial Disclosure, astellas.resultsdisclosure@astellas.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 March 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 March 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate efficacy, safety, pharmacodynamics, and pharmacokinetics of ASP6294 in the treatment of female participants with bladder pain syndrome/interstitial cystitis (BPS/IC).

Protection of trial subjects:

This clinical study was written, conducted and reported in accordance with the protocol, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) Guidelines, and applicable local regulations, including the European Directive 2001/20/EC, on the protection of human rights, and with the ethical principles that have their origin in the Declaration of Helsinki. Astellas ensures that the use and disclosure of protected health information (PHI) obtained during a research study complies with the federal, national and/or regional legislation related to the privacy and protection of personal information.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 September 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Netherlands: 2
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Czech Republic: 7
Country: Number of subjects enrolled	Hungary: 15
Country: Number of subjects enrolled	Latvia: 27
Country: Number of subjects enrolled	Poland: 29
Country: Number of subjects enrolled	Russian Federation: 24
Worldwide total number of subjects	119
EEA total number of subjects	95

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	94
From 65 to 84 years	24
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Female participants ≥ 18 years of age with BPS/IC were enrolled at 26 sites in the European Union and Russian Federation.

Pre-assignment

Screening details:

A total of 209 participants signed informed consent. After screening, eligible participants entered a 2-week run-in period, a total of 90 participants discontinued prior to or during the run-in period. Eligible participants who met inclusion criteria and none of the exclusion criteria were enrolled.

Period 1

Period 1 title	Overall Period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	ASP6294

Arm description:

Participants received 320 mg ASP6294 subcutaneous injection at 4-week intervals at baseline (Day 1/Week 0), Week 4 and Week 8.

Arm type	Experimental
Investigational medicinal product name	ASP6294
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received 320 mg ASP6294 subcutaneous injection at 4-week intervals at baseline (Day 1/Week 0), Week 4 and Week 8.

Arm title	Placebo

Arm description:

Participants received placebo to match 320 mg ASP6294 subcutaneous injection at 4-week intervals at baseline (Day 1/Week 0), Week 4 and Week 8.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received placebo to match 320 mg ASP6294 subcutaneous injection at 4-week intervals at baseline (Day 1/Week 0), Week 4 and Week 8.

Number of subjects in period 1	ASP6294	Placebo
Started	57	62
Treated	56	61
Completed Follow-up	51	57 [1]
Completed	51	59
Not completed	6	3
Consent withdrawn by subject	3	-
Adverse Event	1	1
Miscellaneous	2	1
Lost to follow-up	-	1

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The participants who discontinued treatment could have continued in follow-up.

Baseline characteristics

Reporting groups	
Reporting group title	ASP6294
Reporting group description:	
Participants received 320 mg ASP6294 subcutaneous injection at 4-week intervals at baseline (Day 1/Week 0), Week 4 and Week 8.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo to match 320 mg ASP6294 subcutaneous injection at 4-week intervals at baseline (Day 1/Week 0), Week 4 and Week 8.	

Reporting group values	ASP6294	Placebo	Total
Number of subjects	57	62	119
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	49.4	52.8	
standard deviation	± 15.6	± 16.1	-
Gender categorical Units: Subjects			
Male	0	0	0
Female	57	62	119
Race Units: Subjects			
WHITE	57	62	119
Ethnicity Units: Subjects			
Hispanic or Latino	1	0	1
Not Hispanic or Latino	56	61	117
Not reported	0	1	1
Hunners Lesion Units: Subjects			
Yes	5	4	9
No	52	58	110
Presence of a Nonurological Functional Somatic Syndrome Units: Subjects			
Yes	6	10	16
No	51	52	103
Average Mean Daily Bladder Pain (MDP)			
Participants recorded their MDP each day in the evening into an e-diary. The MDP was the average pain experienced over the past 24 hours. The average MDP was the mean of daily assessments of MDP in the week prior to the visit with at least 5 recordings in that week. MDP was measured using an 11-point Numerical Rating Scale (NRS) ranging from 0 (no bladder pain) to 10 (worst imaginable bladder pain).			
Units: Units on a scale			
arithmetic mean	5.58	5.61	
standard deviation	± 0.96	± 1.25	-

Average Worst Daily Bladder Pain (WDP)			
Participants recorded their WDP each day in the evening into an e-diary. The WDP was the worst pain experienced over the past 24 hours. The average WDP was the mean of daily assessments of WDP in the week prior to the visit with at least 5 recordings in that week. WDP was measured using an 11-point NRS ranging from 0 (no bladder pain) to 10 (worst imaginable bladder pain).			
Units: Units on a scale			
arithmetic mean	6.99	7.04	
standard deviation	± 0.96	± 1.12	-
Bladder Pain/ Interstitial Cystitis Symptom Score (BPIC-SS) Total Score			
BPIC-SS is a psychometrically validated and reliable questionnaire with 8 questions concerning bladder pain over previous 7 days. Question (Q) 1 to Q5 assess urinary symptoms and are rated 0 (never) to 4 (always). Q6 and Q7 assess impact of bladder pain and are rated 0 (not at all) to 4 (a great deal). Q8 assess the worst pain on 0 (no bladder pain) to 10 (worst possible bladder pain) NRS. The BPIC-SS total score is the sum of individual question scores and range from 0 to 38, with higher scores indicating a worse situation. A score of 19 or more represents moderate/severe disease activity.			
Units: Units on a scale			
arithmetic mean	26.4	26.8	
standard deviation	± 3.8	± 3.5	-
Mean Number of Level 3 or 4 Urgency Episodes per 24 hours			
For each micturition episode, participants rated the degree of associated urgency severity according to Patient Perception of Intensity of Urgency Scale (PPIUS) on a 5-point categorical scale ranging from 0 to 4, where 0 = no urgency, 1 = mild urgency, 2 = moderate urgency, 3 = severe urgency, and 4 = urge incontinence. Mean number of Level 3 or 4 urgency episodes was the mean of the recordings of Level 3 or 4 urgency episodes in the 3-day electronic micturition diary in the week prior to the visit.			
Units: Episodes per 24 hours			
arithmetic mean	3.87	4.14	
standard deviation	± 5.09	± 4.35	-
Mean Voiding Frequency per 24 hours			
Mean voiding frequency was the mean of the recordings of voiding frequency in the electronic micturition diary in the week prior to the visit with at least 2 days recorded in that week.			
Units: Voids per 24 hours			
arithmetic mean	13.74	13.33	
standard deviation	± 4.09	± 3.74	-
BPIC-SS Worst Bladder Pain (Question 8) Score			
The BPIC-SS is a psychometrically validated and reliable questionnaire with 8 questions concerning bladder pain over the previous 7 days. Q8 of BPIC-SS assessed the worst pain on a 0 (no bladder pain) to 10 (worst possible bladder pain) NRS. For these characteristics, the number of participants analyzed were 53 and 59 in ASP6294 and Placebo arm, respectively.			
Units: Units on a scale			
log mean	7.58	7.54	
standard deviation	± 1.36	± 1.21	-

End points

End points reporting groups

Reporting group title	ASP6294
Reporting group description:	
Participants received 320 mg ASP6294 subcutaneous injection at 4-week intervals at baseline (Day 1/Week 0), Week 4 and Week 8.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo to match 320 mg ASP6294 subcutaneous injection at 4-week intervals at baseline (Day 1/Week 0), Week 4 and Week 8.	

Primary: Change from Baseline in Average Mean Daily Pain (MDP) Score at Week 12

End point title	Change from Baseline in Average Mean Daily Pain (MDP) Score at Week 12
End point description:	
Participants recorded their MDP each day in the evening into an e-diary. The MDP was the average pain experienced over the past 24 hours. The average MDP was the mean of daily assessments of MDP in the week prior to the visit with at least 5 recordings in that week. MDP was measured using an 11-point Numerical Rating Scale (NRS) ranging from 0 (no bladder pain) to 10 (worst imaginable bladder pain). A negative change indicates a reduction/improvement from baseline. The analysis population was Full Analysis Set (FAS), which consisted of all randomized participants who received ≥ 1 injection of double-blind study drug and had nonmissing MDP values at Visit 2/baseline and ≥ 1 postbaseline visit (i.e., ≥ 5 recordings in any week postbaseline). FAS participants with available data were included in analysis.	
End point type	Primary
End point timeframe:	
Baseline and Week 12	

End point values	ASP6294	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	52		
Units: Units on a scale				
least squares mean (standard error)	-2.34 (± 0.28)	-2.13 (± 0.26)		

Statistical analyses

Statistical analysis title	Change from Baseline Analysis at Week 12
Statistical analysis description:	
Analysis was performed using Mixed-Effect Model Repeated Measures (MMRM) model with treatment group, week (as factor), treatment-by-week interaction, baseline value, baseline-by-week interaction, region (3 regions), nonurological functional somatic syndrome (yes, no) and Hunner's lesions (yes, no). Difference was calculated by subtracting the LS mean of placebo group from the LS mean of ASP6294 group.	
Comparison groups	ASP6294 v Placebo

Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.591
Method	MMRM
Parameter estimate	Least-Squares (LS) Mean Difference
Point estimate	-0.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.84
upper limit	0.43
Variability estimate	Standard error of the mean
Dispersion value	0.38

Secondary: Change from Baseline in Average Worst Daily Pain (WDP) Score at Week 12

End point title	Change from Baseline in Average Worst Daily Pain (WDP) Score at Week 12

End point description:

Participants recorded their WDP each day in the evening into an e-diary. The WDP was the worst pain experienced over the past 24 hours. The average WDP was the mean of daily assessments of WDP in the week prior to the visit with at least 5 recordings in that week. WDP was measured using an 11-point NRS ranging from 0 (no bladder pain) to 10 (worst imaginable bladder pain). A negative change indicates a reduction/improvement from baseline. FAS participants with available data were included in analysis.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	ASP6294	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	52		
Units: Units on a scale				
least squares mean (standard error)	-2.22 (± 0.32)	-2.33 (± 0.30)		

Statistical analyses

Statistical analysis title	Change from Baseline Analysis at Week 12

Statistical analysis description:

Analysis was performed using MMRM model with treatment group, week (as factor), treatment-by-week interaction, baseline value, baseline-by-week interaction, region (3 regions), nonurological functional somatic syndrome (yes, no) and Hunner's lesions (yes, no).
Difference was calculated by subtracting the LS mean of placebo group from the LS mean of ASP6294 group.

Comparison groups	ASP6294 v Placebo

Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.817
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	0.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.63
upper limit	0.84
Variability estimate	Standard error of the mean
Dispersion value	0.44

Secondary: Change From Baseline in Mean Voiding Frequency per 24 hours at Week 12

End point title	Change From Baseline in Mean Voiding Frequency per 24 hours at Week 12

End point description:

Mean voiding frequency was the mean of the recordings of voiding frequency in the electronic micturition diary in the week prior to the visit with at least 2 days recorded in that week. A negative change indicates a reduction/improvement from baseline. FAS participants with available data were included in analysis.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	ASP6294	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: Voids per 24 hours				
least squares mean (standard error)	-2.16 (± 0.65)	-1.15 (± 0.64)		

Statistical analyses

Statistical analysis title	Change from Baseline Analysis at Week 12

Statistical analysis description:

Analysis was performed using MMRM model with treatment group, week (as factor), treatment-by-week interaction, baseline value, baseline-by-week interaction, region (3 regions), nonurological functional somatic syndrome (yes, no) and Hunner's lesions (yes, no).
Difference was calculated by subtracting the LS mean of placebo group from the LS mean of ASP6294 group.

Comparison groups	ASP6294 v Placebo

Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.272
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.01
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.54
upper limit	0.52
Variability estimate	Standard error of the mean
Dispersion value	0.91

Secondary: Change From Baseline in Mean Number of Level 3 or 4 Urgency Episodes (Based on Patient Perception of Intensity of Urgency Scale [PPIUS]) per 24 hours at Week 12

End point title	Change From Baseline in Mean Number of Level 3 or 4 Urgency Episodes (Based on Patient Perception of Intensity of Urgency Scale [PPIUS]) per 24 hours at Week 12

End point description:

The perceived level of urinary urgency was measured using PPIUS. For each micturition episode, participant was asked to rate the degree of associated urgency severity according to PPIUS. PPIUS is a 5-point categorical scale ranging from 0 to 4, where 0 = no urgency (participant felt no need to empty the bladder, but did so for other reasons), 1 = mild urgency (participant could postpone voiding as long as necessary, without fear of wetting herself), 2 = moderate urgency (participant could postpone voiding for a short while, without fear of wetting herself), 3 = severe urgency (participant could not postpone voiding, had to rush to the toilet in order not to wet herself), and 4 = urge incontinence (participant leaked before arriving to the toilet). Mean number of Level 3 or 4 urgency episodes was the mean of recordings of Level 3 or 4 urgency episodes in 3-day electronic micturition diary in the week prior to visit. FAS participants with available data were included in analysis.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	ASP6294	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: Episodes per 24 hours				
least squares mean (standard error)	-1.52 (± 0.51)	-1.84 (± 0.51)		

Statistical analyses

Statistical analysis title	Change from Baseline Analysis at Week 12

Statistical analysis description:

Analysis was performed using MMRM model with treatment group, week (as factor), treatment-by-week

interaction, baseline value, baseline-by-week interaction, region (3 regions), nonurological functional somatic syndrome (yes, no) and Hunner's lesions (yes, no).
Difference was calculated by subtracting the LS mean of placebo group from the LS mean of ASP6294 group.

Comparison groups	ASP6294 v Placebo
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.664
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	0.31
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.89
upper limit	1.51
Variability estimate	Standard error of the mean
Dispersion value	0.72

Secondary: Change From Baseline in Bladder Pain/ Interstitial Cystitis Symptom Score (BPIC-SS) Total Score at Week 12

End point title	Change From Baseline in Bladder Pain/ Interstitial Cystitis Symptom Score (BPIC-SS) Total Score at Week 12

End point description:

The BPIC-SS is a psychometrically validated and reliable questionnaire with 8 questions concerning bladder pain over the previous 7 days. Question (Q) 1 to Q5 assess urinary symptoms (how often urinated because of pain, need to urinate just after previous urination, urination to avoid pain, pressure in the bladder, and pain in the bladder) and are rated 0 (never) to 4 (always). Q6 and Q7 assess the impact of bladder pain (bothered by frequent urination during daytime and nighttime) and are rated 0 (not at all) to 4 (a great deal). Q8 assess the worst pain on a 0 (no bladder pain) to 10 (worst possible bladder pain) NRS. The BPIC-SS total score is the sum of the individual question scores and range from 0 to 38, with higher scores indicating a worse situation. A score of 19 or more represents moderate/severe disease activity. A negative change indicates a reduction/improvement from baseline. FAS participants with available data were included in analysis.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	ASP6294	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	54		
Units: Units on a scale				
least squares mean (standard error)	-7.41 (± 1.13)	-7.16 (± 1.07)		

Statistical analyses

Statistical analysis title	Change from Baseline Analysis at Week 12

Statistical analysis description:

Analysis was performed using MMRM model with treatment group, week (as factor), treatment-by-week interaction, baseline value, baseline-by-week interaction, region (3 regions), nonurological functional somatic syndrome (yes, no) and Hunner's lesions (yes, no).
Difference was calculated by subtracting the LS mean of placebo group from the LS mean of ASP6294 group.

Comparison groups	ASP6294 v Placebo
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.872
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.25
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.84
upper limit	2.33
Variability estimate	Standard error of the mean
Dispersion value	1.56

Secondary: Change From Baseline in BPIC-SS Worst Bladder Pain (Question 8) Score at Week 12

End point title	Change From Baseline in BPIC-SS Worst Bladder Pain (Question 8) Score at Week 12

End point description:

The BPIC-SS is a psychometrically validated and reliable questionnaire with 8 questions concerning bladder pain over the previous 7 days. Q8 of BPIC-SS assess the worst pain on a 0 (no bladder pain) to 10 (worst possible bladder pain) NRS. A negative change indicates a reduction/improvement from baseline. FAS participants with available data were included in analysis.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	ASP6294	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	54		
Units: Units on a scale				
least squares mean (standard error)	-2.35 (± 0.36)	-2.38 (± 0.34)		

Statistical analyses

Statistical analysis title	Change from Baseline Analysis at Week 12

Statistical analysis description:

Analysis was performed using MMRM model with treatment group, week (as factor), treatment-by-week interaction, baseline value, baseline-by-week interaction, region (3 regions), nonurological functional somatic syndrome (yes, no) and Hunner's lesions (yes, no).
Difference was calculated by subtracting the LS mean of placebo group from the LS mean of ASP6294 group.

Comparison groups	ASP6294 v Placebo
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.956
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	0.03
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.79
upper limit	0.84
Variability estimate	Standard error of the mean
Dispersion value	0.49

Secondary: Percentage of Participants With Moderately Improved or Better Grade on the Global Response Assessment (GRA) at Week 12

End point title	Percentage of Participants With Moderately Improved or Better Grade on the Global Response Assessment (GRA) at Week 12

End point description:

A self-reported 7 grade GRA was used to evaluate a participant's clinical condition relative to baseline. The GRA read: As compared to when the participant started the study, how would the participant rate the participant's overall symptoms now? The 7 GRA grades were "markedly worse", "moderately worse", "slightly worse", "no change", "slightly improved", "moderately improved" or "markedly improved". Percentage of participants with a successful GRA response (defined as the response of "moderately improved" or better ["markedly improved"] are reported. FAS participants with available data were included in analysis.

End point type	Secondary

End point timeframe:

Week 12

End point values	ASP6294	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	54		
Units: percentage of participants				
number (confidence interval 90%)	40.6 (29.6 to 52.7)	32.9 (23.3 to 44.3)		

Statistical analyses

Statistical analysis title	Moderately Improved or Better Grade on GRA

Statistical analysis description:

Analysis was performed using a logistic regression model with treatment group, region (3 regions), nonurological functional somatic syndrome (yes, no) and Hunner's lesions (yes, no).

Comparison groups	ASP6294 v Placebo
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.426
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.394
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.702
upper limit	2.767

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From the first administration of study drug until Week 18	
Adverse event reporting additional description:	
Safety analysis set (SAF) consisted of all participants who received ≥ 1 injection of double-blind study drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups	
Reporting group title	ASP6294
Reporting group description:	
Participants received 320 mg ASP6294 subcutaneous injection at 4-week intervals at baseline (Day 1/Week 0), Week 4 and Week 8.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo to match 320 mg ASP6294 subcutaneous injection at 4-week intervals at baseline (Day 1/Week 0), Week 4 and Week 8.	

Serious adverse events	ASP6294	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 56 (0.00%)	3 / 61 (4.92%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Vaginal cancer			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cervicobrachial syndrome			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Musculoskeletal pain			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Diverticulitis			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	ASP6294	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 56 (14.29%)	5 / 61 (8.20%)	
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 56 (8.93%)	2 / 61 (3.28%)	
occurrences (all)	9	2	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 56 (7.14%)	2 / 61 (3.28%)	
occurrences (all)	6	4	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	3 / 56 (5.36%)	1 / 61 (1.64%)	
occurrences (all)	4	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 June 2017	The changes included: 1) Added information for Data Safety Monitoring Board throughout the protocol. 2) Addition of inclusion criterion: Participants must have tried 2 previous therapies for BPS/IC with unsatisfactory results, prior to study entry. 3) Inclusion criterion number 9 was reworded to participants must agree not to donate ova at screening and throughout the study period.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported