Clinical trial results:
A phase 3b, open-label pilot study to evaluate the safety and effectiveness of up to four treatment cycles of AA4500 in combination with the ErecAid® Esteem® Manual Vacuum Therapy System in men with Peyronie's disease.

Summary

EudraCT number	2013-005384-66
Trial protocol	GB
Global end of trial date	09 March 2016

Results information

Result version number	v1 (current)
This version publication date	01 December 2016
First version publication date	01 December 2016

Trial information

Trial identification

Sponsor protocol code	AUX-CC-807

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Auxilium Pharmaceuticals, LLC
Sponsor organisation address	1400 Atwater Drive, Malvern, United States, 19355
Public contact	Director, Regulatory Affairs, Endo Ventures Limited, 00353 1 268 2017, Walsh.Ciara@endo.com
Scientific contact	Director, Regulatory Affairs, Endo Ventures Limited, 00353 1 268 2017, Walsh.Ciara@endo.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	09 March 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 March 2016
Global end of trial reached?	Yes
Global end of trial date	09 March 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objectives of this study are to assess the safety and effectiveness of AA4500 in combination with the ErecAid® Esteem® Manual Vacuum Therapy System in improving curvature deformity in men with Peyronie's disease.

Protection of trial subjects:

Use of Vacuum System
Prior to first use of the vacuum system, the Investigator or qualified designee instructed each subject in the proper usage of the ErecAid Esteem Manual Vacuum Therapy System. Each subject demonstrated to the Investigator/qualified designee that he could safely and correctly use the vacuum system before he was permitted to start therapy.
Penile Anesthesia
Before each injection of AA4500, the Investigator could administer a dorsal and/or a circumferential penile block according to the practice of his/her institution and the subject's willingness to receive penile anesthesia. If preferred, topical anesthesia (eg, EMLA cream) could be applied before injection. Anesthesia was supplied by the Investigator and administered in accordance with the pharmacy practices at the institution.
Care Procedures After Injection
Immediately after injection, the Investigator or qualified designee (qualified by license, education, and training to perform the study procedure according to local, state, and country requirements) applied pressure to the injection site for 3 minutes and instructed the subject to continue applying pressure for another 5 minutes. Additionally, to evaluate the subject for possible immediate immunological AEs, the subject remained in direct observation of medical personnel who were skilled in the management of acute allergic reactions for the first 20 minutes after receiving an injection of study drug
Because AA4500 is a foreign protein, an antibody response was measured in all subjects following treatment.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 September 2014
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 Kingdom: 30
Worldwide total number of subjects	30
EEA total number of subjects	30

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)	22
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects were screened for study eligibility within 21 days before the initial injection of study drug in the first treatment cycle. Enrollment included 30 AA4500 naïve subjects who met the eligibility criteria.

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	AA4500 0.58 mg with Investigator Modeling

Arm description:

2 injections separated by approximately 24 to 72 hours, repeated after 42 days (±5 days) for up to 4 treatment cycles
Approximately 24 to 72 hours after the final injection of each treatment cycle the Investigator or qualified designee modeled the plaque.
Fourteen days (+/- 2 days) after the second injection of each treatment cycle, subject would initiate use of the vacuum device twice daily until the next treatment visit; and through Week 24 after the last treatment cycle.

Arm type	Experimental
Investigational medicinal product name	XIAFLEX/XIAPEX
Investigational medicinal product code	AA4500 (now EN3835)
Other name	Collagenase, Clostridium histolyticum
Pharmaceutical forms	Injection
Routes of administration	Intralesional use

Dosage and administration details:

AA4500 was administered only after reconstitution with diluent (0.9% NaCl containing 0.03% calcium chloride). The volume of injection was 0.25 mL. AA4500 was injected directly into the primary penile plaque (at the point of maximal concavity as marked) of the flaccid penis according to instructions provided in the protocol. During each treatment cycle, subjects received 2 injections of study drug with approximately 24 to 72 hours between injections. Subjects could receive up to 4 treatment cycles; each cycle separated by 42 days (±5 days).

Arm title	AA4500 0.58 mg without Investigator Modeling

Arm description:

2 injections separated by approximately 24 to 72 hours, repeated after 42 days (±5 days) for up to 4 treatment cycles.
Fourteen days (+/- 2 days) after the second injection of each treatment cycle, subject would initiate use of the vacuum device twice daily until the next treatment visit; and through Week 24 after the last treatment cycle.

Arm type	Experimental
Investigational medicinal product name	XIAFLEX/XIAPEX
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Dosage and administration details:

AA4500 was administered only after reconstitution with diluent (0.9% NaCl containing 0.03% calcium chloride). The volume of injection was 0.25 mL. AA4500 was injected directly into the primary penile

plaque (at the point of maximal concavity as marked) of the flaccid penis according to instructions provided in the protocol. During each treatment cycle, subjects received 2 injections of study drug with approximately 24 to 72 hours between injections. Subjects could receive up to 4 treatment cycles; each cycle separated by 42 days (±5 days).

Number of subjects in period 1	AA4500 0.58 mg with Investigator Modeling	AA4500 0.58 mg without Investigator Modeling
Started	15	15
Completed	15	15

Period 2

Period 2 title	Week 36
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	AA4500 0.58 mg with Investigator Modeling

Arm description:

2 injections separated by approximately 24 to 72 hours, repeated after 42 days (±5 days) for up to 4 treatment cycles
Approximately 24 to 72 hours after the final injection of each treatment cycle the Investigator or qualified designee modeled the plaque.
Fourteen days (+/- 2 days) after the second injection of each treatment cycle, subject would initiate use of the vacuum device twice daily until the next treatment visit; and through Week 24 after the last treatment cycle.

Arm type	Experimental
Investigational medicinal product name	XIAFLEX/XIAPEX
Investigational medicinal product code	AA4500 (now EN3835)
Other name	Collagenase, Clostridium histolyticum
Pharmaceutical forms	Injection
Routes of administration	Intralesional use

Dosage and administration details:

AA4500 was administered only after reconstitution with diluent (0.9% NaCl containing 0.03% calcium chloride). The volume of injection was 0.25 mL. AA4500 was injected directly into the primary penile plaque (at the point of maximal concavity as marked) of the flaccid penis according to instructions provided in the protocol. During each treatment cycle, subjects received 2 injections of study drug with approximately 24 to 72 hours between injections. Subjects could receive up to 4 treatment cycles; each cycle separated by 42 days (±5 days).

Arm title	AA4500 0.58 mg without Investigator Modeling

Arm description:

2 injections separated by approximately 24 to 72 hours, repeated after 42 days (±5 days) for up to 4 treatment cycles.
Fourteen days (+/- 2 days) after the second injection of each treatment cycle, subject would initiate use of the vacuum device twice daily until the next treatment visit; and through Week 24 after the last treatment cycle.

Arm type	Experimental
Investigational medicinal product name	XIAFLEX/XIAPEX
Investigational medicinal product code	AA4500 (now EN3835)
Other name	Collagenase, Clostridium histolyticum
Pharmaceutical forms	Injection
Routes of administration	Intralesional use

Dosage and administration details:

AA4500 was administered only after reconstitution with diluent (0.9% NaCl containing 0.03% calcium chloride). The volume of injection was 0.25 mL. AA4500 was injected directly into the primary penile plaque (at the point of maximal concavity as marked) of the flaccid penis according to instructions provided in the protocol. During each treatment cycle, subjects received 2 injections of study drug with approximately 24 to 72 hours between injections. Subjects could receive up to 4 treatment cycles; each cycle separated by 42 days (±5 days).

Number of subjects in period 2	AA4500 0.58 mg with Investigator Modeling	AA4500 0.58 mg without Investigator Modeling
Started	15	15
Completed	13	12
Not completed	2	3
Protocol deviation	2	3

Baseline characteristics

Reporting groups

Reporting group title	AA4500 0.58 mg with Investigator Modeling

Reporting group description:

2 injections separated by approximately 24 to 72 hours, repeated after 42 days (±5 days) for up to 4 treatment cycles
Approximately 24 to 72 hours after the final injection of each treatment cycle the Investigator or qualified designee modeled the plaque.
Fourteen days (+/- 2 days) after the second injection of each treatment cycle, subject would initiate use of the vacuum device twice daily until the next treatment visit; and through Week 24 after the last treatment cycle.

Reporting group title	AA4500 0.58 mg without Investigator Modeling

Reporting group description:

2 injections separated by approximately 24 to 72 hours, repeated after 42 days (±5 days) for up to 4 treatment cycles.
Fourteen days (+/- 2 days) after the second injection of each treatment cycle, subject would initiate use of the vacuum device twice daily until the next treatment visit; and through Week 24 after the last treatment cycle.

Reporting group values	AA4500 0.58 mg with Investigator Modeling	AA4500 0.58 mg without Investigator Modeling	Total
Number of subjects	15	15	30
Age categorical Units: Subjects			
< 45 years	2	1	3
45-64 years	8	11	19
65 years and over	5	3	8
Age continuous Units: years			
arithmetic mean	57.8	57.6	
standard deviation	± 9.37	± 8.44	-
Gender categorical Units: Subjects			
Male	15	15	30

End points

End points reporting groups

Reporting group title	AA4500 0.58 mg with Investigator Modeling

Reporting group description:

2 injections separated by approximately 24 to 72 hours, repeated after 42 days (±5 days) for up to 4 treatment cycles
Approximately 24 to 72 hours after the final injection of each treatment cycle the Investigator or qualified designee modeled the plaque.
Fourteen days (+/- 2 days) after the second injection of each treatment cycle, subject would initiate use of the vacuum device twice daily until the next treatment visit; and through Week 24 after the last treatment cycle.

Reporting group title	AA4500 0.58 mg without Investigator Modeling

Reporting group description:

2 injections separated by approximately 24 to 72 hours, repeated after 42 days (±5 days) for up to 4 treatment cycles.
Fourteen days (+/- 2 days) after the second injection of each treatment cycle, subject would initiate use of the vacuum device twice daily until the next treatment visit; and through Week 24 after the last treatment cycle.

Reporting group title	AA4500 0.58 mg with Investigator Modeling

Reporting group description:

2 injections separated by approximately 24 to 72 hours, repeated after 42 days (±5 days) for up to 4 treatment cycles
Approximately 24 to 72 hours after the final injection of each treatment cycle the Investigator or qualified designee modeled the plaque.
Fourteen days (+/- 2 days) after the second injection of each treatment cycle, subject would initiate use of the vacuum device twice daily until the next treatment visit; and through Week 24 after the last treatment cycle.

Reporting group title	AA4500 0.58 mg without Investigator Modeling

Reporting group description:

2 injections separated by approximately 24 to 72 hours, repeated after 42 days (±5 days) for up to 4 treatment cycles.
Fourteen days (+/- 2 days) after the second injection of each treatment cycle, subject would initiate use of the vacuum device twice daily until the next treatment visit; and through Week 24 after the last treatment cycle.

Primary: Percent Change from Baseline in Penile Curvature at Week 36 (LOCF)

End point title	Percent Change from Baseline in Penile Curvature at Week 36 (LOCF)

End point description:

Percent change from baseline in penile curvature at day 252/week 36. After administration of a PGE1 to induce an erection, the investigator or qualified designee measured the angle of penile deformity three times with a goniometer protractor device using a standard method. All three measurements had to be within 10° of each other; the most severe of the three findings was recorded.

End point type	Primary

End point timeframe:

Week 36

End point values	AA4500 0.58 mg with Investigator Modeling	AA4500 0.58 mg without Investigator Modeling		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: % change from baseline				
arithmetic mean (standard deviation)	-39.3 (± 13.21)	-41.1 (± 11.51)		

Statistical analyses

Statistical analysis title	Treatment comparison
Statistical analysis description:	
Treatment comparisons: Least square mean difference and its 95% CI	
Comparison groups	AA4500 0.58 mg with Investigator Modeling v AA4500 0.58 mg without Investigator Modeling
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other[1]
Parameter estimate	Difference of the means
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.5
upper limit	11

Notes:

[1] - 95% CIs for the difference of means between treatment groups were estimated using analysis of variance (ANOVA) with a factor of treatment group.
LOCF is the last known observation carried forward to week 36 if week 36 measurement was missing.

Secondary: Change from Baseline in PDQ Peyronie's Disease Bother Domain

End point title	Change from Baseline in PDQ Peyronie's Disease Bother Domain
End point description:	
Change from baseline in the Peyronie's disease bother domain (PDQ questions 10-15). Each subject completed the PDQ questions 10-15.	
End point type	Secondary
End point timeframe:	
Week 36	

End point values	AA4500 0.58 mg with Investigator Modeling	AA4500 0.58 mg without Investigator Modeling		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	11		
Units: PDQ Peyronie's Disease Bother Domain				
arithmetic mean (standard deviation)	-2.4 (± 2.53)	-3.8 (± 2.99)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in PDQ Peyronie's Disease Physical and Psychological Symptom Domain

End point title	Change from Baseline in PDQ Peyronie's Disease Physical and Psychological Symptom Domain

End point description:

Change from baseline in severity of Peyronie's disease physical and psychological symptom domain (PDQ questions 1-6). Each subject completed PDQ questions 1-6.

End point type	Secondary

End point timeframe:

Week 36

End point values	AA4500 0.58 mg with Investigator Modeling	AA4500 0.58 mg without Investigator Modeling		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	11		
Units: PDQ PD Physical and Psychological				
arithmetic mean (standard deviation)	-2.2 (± 4.38)	-6.4 (± 2.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in PDQ Penile Pain Domain

End point title	Change from Baseline in PDQ Penile Pain Domain

End point description:

Change from baseline in the penile pain domain (PDQ questions 7-9). Each subject completed PDQ questions 7-9.

End point type	Secondary

End point timeframe:

Week 36

End point values	AA4500 0.58 mg with Investigator Modeling	AA4500 0.58 mg without Investigator Modeling		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	11		
Units: PDQ Penile Pain Domain				
arithmetic mean (standard deviation)	0.7 (± 3.07)	-1.3 (± 3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Responder Analysis Based on Global Assessment of Peyronie's Disease

End point title	Responder Analysis Based on Global Assessment of Peyronie's Disease

End point description:

Responder analysis based on subject global assessment (a responder was a subject with a score of at least +1 on the subject global assessment). Each subject was asked to assess the overall change (much improved to much worse) in the symptoms and effects of Peyronie's disease on his life.

End point type	Secondary

End point timeframe:

Week 36

End point values	AA4500 0.58 mg with Investigator Modeling	AA4500 0.58 mg without Investigator Modeling		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	13		
Units: Responder				
yes	13	12		
no	2	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Composite Responder Analysis Based on Penile Curvature and Peyronie's Disease Bother Domain Score

End point title	Composite Responder Analysis Based on Penile Curvature and Peyronie's Disease Bother Domain Score

End point description:

Composite responder analysis based on percentage change in penile curvature and change in PDQ bother score (a composite responder was a subject with a at least 20% reduction from baseline in penile curvature and 1 or more reduction in PDQ bother score).

End point type	Secondary

End point timeframe:
Week 36

End point values	AA4500 0.58 mg with Investigator Modeling	AA4500 0.58 mg without Investigator Modeling		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	13		
Units: Composite Responders				
yes	10	11		
no	5	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Penile Plaque Consistency

End point title	Change from Baseline in Penile Plaque Consistency

End point description:

Change from baseline in penile plaque consistency.
The investigator or qualified designee determined the consistency of the primary plaque in the flaccid penis as hard [solid] =5; firm throughout =4; moderate firmness =3; soft =2; or non-palpable =1.
For non-homogeneous plaques, the investigator gave his/her opinion as to which of the categories listed above best describes the plaque.

End point type	Secondary

End point timeframe:
Week 36

End point values	AA4500 0.58 mg with Investigator Modeling	AA4500 0.58 mg without Investigator Modeling		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: Penile Plaque Consistency				
arithmetic mean (standard deviation)	-0.4 (± 0.51)	-0.1 (± 0.52)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Penile Length

End point title	Change from Baseline in Penile Length

End point description:

The investigator or qualified designee measured the length of the stretched flaccid penis. The measurement was obtained by compressing the fat pad to the pubis and measuring dorsally on full stretch to the corona with a centimeter ruler.

End point type	Secondary

End point timeframe:

Week 36

End point values	AA4500 0.58 mg with Investigator Modeling	AA4500 0.58 mg without Investigator Modeling		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: Penile Length (cm)				
arithmetic mean (standard deviation)	0.23 (± 0.598)	0.64 (± 0.579)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in IIEF Erectile Function

End point title	Change from Baseline in IIEF Erectile Function

End point description:

Change from baseline in erectile function domain score of the IIEF. Each of the 15 questions contained in the IIEF questionnaire were rated by the subject on a numerical scale of 0 (worst) to 5 (best).

End point type	Secondary

End point timeframe:

Week 36

End point values	AA4500 0.58 mg with Investigator Modeling	AA4500 0.58 mg without Investigator Modeling		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: IIEF Domain total score				
arithmetic mean (standard deviation)	-2.8 (± 10.42)	1.9 (± 5.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in IIEF Orgasmic Function

End point title	Change from Baseline in IIEF Orgasmic Function

End point description:

Change from baseline in orgasmic function domain score of the IIEF. Each of the 15 questions contained in the IIEF questionnaire were rated by the subject on a numerical scale of 0 (worst) to 5 (best).

End point type	Secondary

End point timeframe:

Week 36

End point values	AA4500 0.58 mg with Investigator Modeling	AA4500 0.58 mg without Investigator Modeling		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	12		
Units: IIEF Domain Total Score				
arithmetic mean (standard deviation)	-1 (± 4.11)	-0.3 (± 2.64)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in IIEF Sexual Desire

End point title	Change from Baseline in IIEF Sexual Desire

End point description:

Change from baseline in sexual desire domain score of the IIEF. Each of the 15 questions contained in the IIEF questionnaire were rated by the subject on a numerical scale of 0 (worst) to 5 (best).

End point type	Secondary

End point timeframe:

Week 36

End point values	AA4500 0.58 mg with Investigator Modeling	AA4500 0.58 mg without Investigator Modeling		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	13		
Units: IIEF Domain Total Score				
arithmetic mean (standard deviation)	-0.3 (± 1.62)	-0.1 (± 1.38)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in IIEF Intercourse Satisfaction

End point title	Change from Baseline in IIEF Intercourse Satisfaction

End point description:

Change from baseline in intercourse satisfaction domain score of the IIEF. Each of the 15 questions contained in the IIEF questionnaire were rated by the subject on a numerical scale of 0 (worst) to 5 (best).

End point type	Secondary

End point timeframe:

Week 36

End point values	AA4500 0.58 mg with Investigator Modeling	AA4500 0.58 mg without Investigator Modeling		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	12		
Units: IIEF Domain Total Score				
arithmetic mean (standard deviation)	-0.8 (± 4.46)	0.8 (± 5.45)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in IIEF Overall Satisfaction

End point title	Change from Baseline in IIEF Overall Satisfaction

End point description:

Change from baseline in overall satisfaction domain score of the IIEF. Each of the 15 questions contained in the IIEF questionnaire were rated by the subject on a numerical scale of 0 (worst) to 5 (best).

End point type	Secondary

End point timeframe:

Week 36

End point values	AA4500 0.58 mg with Investigator Modeling	AA4500 0.58 mg without Investigator Modeling		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	13		
Units: IIEF Domain Total Score				
arithmetic mean (standard deviation)	0.3 (± 1.79)	2 (± 2.61)		

Statistical analyses

No statistical analyses for this end point

Secondary: Direction of Penile Curvature

End point title	Direction of Penile Curvature

End point description:

The investigator or qualified designee determined the primary direction of penile curvature as right lateral, right dorsolateral, dorsal, left dorsolateral, or left lateral. Subjects with ventral curvature were excluded from the study.

End point type	Secondary

End point timeframe:

Week 36

End point values	AA4500 0.58 mg with Investigator Modeling	AA4500 0.58 mg without Investigator Modeling		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: participants				
Right Lateral	1	0		
Right Dorsolateral	0	0		
Dorsal	5	5		
Left Dorsolateral	7	7		
Left Lateral	0	0		
Ventral	0	0		
Not Done	2	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Penile Plaques

End point title	Number of Penile Plaques

End point description:

The investigator or qualified designee located and documented the number of plaque(s) within the stretched flaccid penis.

End point type	Secondary

End point timeframe:

Week 36

End point values	AA4500 0.58 mg with Investigator Modeling	AA4500 0.58 mg without Investigator Modeling		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: participants				
None	0	0		
One	11	11		
Two	1	1		
More Than Two	1	0		
Not Done	2	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Penile Pain on Palpitation

End point title	Penile Pain on Palpitation

End point description:

The investigator or qualified designee documented penile pain on palpation of the flaccid penis as none, mild, moderate, or severe.

End point type	Secondary

End point timeframe:

Week 36

End point values	AA4500 0.58 mg with Investigator Modeling	AA4500 0.58 mg without Investigator Modeling		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: participants				
None	13	12		
Mild	0	0		
Moderate	0	0		
Severe	0	0		
Not Done	2	3		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Throughout the study, the Investigator monitored each subject for evidence of drug intolerance and for the development of clinical and/or laboratory evidence of an AE. An AE assessment was made by the Investigator on a routine basis throughout the study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	AA4500 0.58 mg with Investigator Modeling
Reporting group description: -	
Reporting group title	AA4500 0.58 mg without Investigator Modeling

Reporting group description: -

Serious adverse events	AA4500 0.58 mg with Investigator Modeling	AA4500 0.58 mg without Investigator Modeling	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 15 (13.33%)	0 / 15 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Pericarditis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	AA4500 0.58 mg with Investigator Modeling	AA4500 0.58 mg without Investigator Modeling	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 15 (100.00%)	15 / 15 (100.00%)	

Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Injection site swelling			
subjects affected / exposed	1 / 15 (6.67%)	2 / 15 (13.33%)	
occurrences (all)	1	2	
Nodule			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Local swelling			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Injection site pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Suprapubic pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Injection site bruising			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Malaise			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Needle issue			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Injection site discomfort			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Penile swelling			
subjects affected / exposed	11 / 15 (73.33%)	15 / 15 (100.00%)	
occurrences (all)	21	29	

Penile pain			
subjects affected / exposed	8 / 15 (53.33%)	5 / 15 (33.33%)	
occurrences (all)	14	6	
Penile erythema			
subjects affected / exposed	0 / 15 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Erectile dysfunction			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Erection increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Dyspareunia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Scrotal haematocoele			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Penile blister			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Penile oedema			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Penis disorder			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Investigations			
Eosinophil count increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			

Penile contusion subjects affected / exposed occurrences (all)	13 / 15 (86.67%) 29	15 / 15 (100.00%) 29	
Contusion subjects affected / exposed occurrences (all)	3 / 15 (20.00%) 3	2 / 15 (13.33%) 2	
Subcutaneous haematoma subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 15 (6.67%) 1	
Ligament sprain subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 15 (0.00%) 0	
Nervous system disorders Epilepsy subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 15 (0.00%) 0	
Ear and labyrinth disorders Tinnitus subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 15 (0.00%) 0	
Gastrointestinal disorders Inguinal hernia subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 15 (0.00%) 0	
Skin and subcutaneous tissue disorders Skin discolouration subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 15 (6.67%) 1	
Psoriasis subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 15 (0.00%) 0	
Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 15 (0.00%) 0	
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	2 / 15 (13.33%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 15 (6.67%)	2 / 15 (13.33%)	
occurrences (all)	1	2	
Upper respiratory tract infection	Additional description: 1 occurrence of Upper respiratory tract infection in the AA4500 0.58 mg without Investigator Modeling group was a non-TEAE.		
subjects affected / exposed	0 / 15 (0.00%)	3 / 15 (20.00%)	
occurrences (all)	0	4	
Conjunctivitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Lower respiratory tract infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported