THE JOURNAL OF
SEXUAL MEDICINE

ORIGINAL RESEARCH

PEYRONIE'S DISEASE

Treatment of Peyronie's Disease With Collagenase *Clostridium histolyticum* and Vacuum Therapy: A Randomized, Open-Label Pilot Study

David J. Ralph, FRCS,[1] Amr Abdel Raheem, PhD,[1,2] and Genzhou Liu, PhD[3]

ABSTRACT

Background: Collagenase *Clostridium histolyticum* (CCH) is indicated for the treatment of penile curvature in adult men with Peyronie's disease (PD) with palpable plaque and curvature deformity of at least 30° at the start of therapy.

Aim: To evaluate the efficacy and safety of CCH plus vacuum-pump therapy with and without penile modeling for the management of PD.

Methods: Adult men with PD and penile curvature of at least 30° were randomly assigned to receive CCH 0.58 mg plus vacuum therapy alone (n = 15) or with penile plaque modeling (n = 15). Patients received no more than four treatment cycles (cycle = ~6-week duration), each consisting of two intralesional injections of CCH administered 24 to 72 hours apart. Vacuum therapy was applied twice daily from 14 days after the second injection of each cycle until the following cycle. Modeling was performed 24 to 72 hours after the second injection of each cycle.

Outcomes: The primary end point was change in penile curvature from baseline to week 36; additional end points included changes in Peyronie's Disease Questionnaire (PDQ) domain scores, composite response (≥20% decrease in penile curvature and decrease in PDQ bother score ≥ 1 point), and global response (small but important, moderate, or much improvement in the Global Assessment of PD).

Results: At week 36, improvement in penile curvature from baseline was similar in the two groups (mean change from baseline = −23.7° [SD = 10.9] for CCH + vacuum + modeling and −23.3° [SD = 7.2] for CCH + vacuum; between-group difference = −0.3°, 95% CI = −7.3 to 6.6). Improvements in most PDQ domains, including bother, were observed from baseline to week 36 in the two groups. Most patients were composite (66.7% and 84.6% with CCH + vacuum + modeling and CCH + vacuum, respectively) and global (86.7% and 92.3%, respectively) responders. The most common adverse events were penile contusion, penile swelling, and penile pain.

Clinical Implications: Vacuum-pump therapy administered alone or in combination with modeling after CCH treatment could improve PD symptoms.

Strengths and Limitations: This was a pilot study with a small sample and limited follow-up duration.

Conclusion: CCH and vacuum-pump therapy (alone or combined with modeling) could be an appropriate consideration for men with PD and warrants further investigation. **Ralph DJ, Abdel Raheem A, Liu G. Treatment of Peyronie's Disease With Collagenase *Clostridium histolyticum* and Vacuum Therapy: A Randomized, Open-Label Pilot Study. J Sex Med 2017;14:1430−1437.**

Key Words: Collagenase; Modeling; Penile Fibromatosis; Male Urogenital Diseases; Hand-Operated Vacuum-Pump Therapy

Received April 13, 2017. Accepted August 31, 2017.

[1]Institute of Urology, University College London Hospitals, London, UK;

[2]Andrology Department, Cairo University Hospital, Cairo, Egypt;

[3]Endo Pharmaceuticals, Inc, Malvern, PA, USA

http://dx.doi.org/10.1016/j.jsxm.2017.08.015

INTRODUCTION

Peyronie's disease (PD) is a fibrotic disorder of the penis that is believed to develop as a response to abnormal wound healing after trauma or microtrauma.[1] PD is characterized by fibrosis of the tunica albuginea, which results in the formation of plaque and the development of penile deformity (particularly curvature) that

might or might not be accompanied by pain.[1,2] Although once considered a rare condition, the current prevalence of PD could be as high as approximately 20%, depending on how the condition is defined and the population is studied.[2] The symptoms of PD, and the potential effect of the condition on erectile function, can cause marked psychosocial stress.[3] Importantly, in most cases, this stress persists throughout the course of the disease, indicating that men with PD do not naturally adapt to the psychological distress associated with the condition.[3] The management of stable PD consists of different pharmacologic and surgical approaches, depending on the severity of the penile deformity and associated symptoms.[1] Surgery is often reserved for the most serious cases[4]; however, evidence to support the efficacy of most current noninvasive or minimally invasive therapies is limited.[1,4]

Collagenase *Clostridium histolyticum* (CCH; Xiaflex, Endo Pharmaceuticals, Inc, Malvern, PA, USA) is a purified mixture of AUX-I and AUX-II collagenases from *C histolyticum* that hydrolyses collagen under physiologic conditions and results in lysis of collagen plaques.[5] CCH has been approved by the US Food and Drug Administration for the treatment of adult men with PD who have palpable collagenous plaques and penile curvature of at least 30° at the start of treatment. In a combined analysis of data from two large randomized, double-blinded, placebo-controlled trials, IMPRESS I and II, treatment with CCH resulted in a mean decrease in penile curvature of 34% compared with 18.2% in patients who received placebo ($P < .0001$).[4] In addition, CCH treatment was associated with significant improvements compared with placebo in the physical and psychological symptoms of PD.[4] Based on these findings, the American Urological Association has included CCH in its guidelines, to be used in combination with penile plaque remodeling, for the decrease of penile curvature in patients with stable PD, penile curvature of 30° to 90°, and intact erectile function.[2]

Another treatment strategy that has been shown to be potentially efficacious in decreasing penile curvature in patients with PD is vacuum-pump therapy.[6] Hence, the present pilot study was performed to investigate the effect of vacuum-pump therapy, with and without penile modeling, on the efficacy and safety of CCH administration for the management of PD.

METHODS

Study Design

The study was a prospective, randomized, open-label, pilot study conducted at a single site in the United Kingdom from October 2014 through March 2016 (ClinicalTrials.gov identifier NCT02267460). The study was conducted according to Good Clinical Practice guidelines and the principles of the Declaration of Helsinki, and the protocol was approved by the appropriate independent ethics committee.

Patients

Men (age $\geq$ 18 years) with stable symptomatic PD, as determined by the investigator, were eligible for inclusion if they had penile curvature of at least 30° in the dorsal, lateral, or dorsolateral plane and if it was possible to delineate the plane of maximal curvature. Principal exclusion criteria included penile curvature less than 30° or greater than 90° at screening; other penile disorders such as hourglass deformity, compromised penile hemodynamics, or significant erectile dysfunction that had failed to respond to oral phosphodiesterase type 5 inhibitors; history of spontaneous priapism; calcified plaque that would preclude correct administration of CCH; receipt of previous oral or intralesional medical therapies for PD within 3 months of the first dose of study drug or the use of mechanical devices within 2 weeks of screening; and previous surgery for PD. Written informed consent was obtained from all patients before inclusion in the study.

Treatments

Once patients met the entry criteria, an investigator requested randomization of the patients into treatment groups through an interactive web response system. Patients were stratified according to the degree of baseline penile curvature (30−60° or >60°) and randomly assigned (1:1), through an interactive web response system using a computer-generated randomization allocation sequence with a block size of 4, to receive CCH plus vacuum-pump therapy with investigator-administered plaque modeling or CCH plus vacuum-pump therapy alone. Because of the nature of the interventions, no blinding took place. Each treatment cycle consisted of two intralesional injections of CCH 0.58 mg separated by approximately 24 to 72 hours. Injections were given directly into the primary penile plaque. Up to four approximately 6-week treatment cycles (ie, eight injections) could be given, with intervals of 42 $\pm$ 5 days between cycles, if penile curvature of at least 15° remained and the investigator considered that further treatment was clinically indicated.

Vacuum-pump therapy was performed using the ErecAid Esteem manual vacuum therapy system (Timm Medical Technologies, Inc, Fort Washington, PA, USA). Patients were instructed to use the pump twice daily (morning and evening) from 14 $\pm$ 2 days after the second injection of CCH in each treatment cycle until the start of the next cycle. Vacuum-pump therapy was continued until the first follow-up visit (nominal week 24). Before the first use of the system, all patients received training in the correct operation of the system and were required to demonstrate that they could use the system safely and correctly. For each application of vacuum therapy, a vacuum was created for 5 to 10 seconds until an adequate erection was obtained. Tension rings or other devices were not used to aid erection. Once the penis was erect, the vacuum was maintained for 30 seconds before release. These steps were performed five times during each treatment session.

Plaque modeling by the investigator or other designated personnel was performed 24 to 72 hours after the second injection of CCH in each treatment cycle. Local anesthesia before modeling was given if requested by the patient. During modeling, the investigator grasped the hardened portion or

plaque of the non-erect penis approximately 1 cm on either side of the site of injection and applied steady pressure to elongate and stretch the penis. This pressure was held for 30 seconds and then released. This procedure was repeated twice at 30-second intervals. Patients did not perform modeling at home.

Assessments

Penile curvature was measured before the administration of CCH at the beginning of each treatment cycle and during follow-up visits at nominal weeks 24 and 36. Curvature was measured three times after prostaglandin E_1 induction of an erection using a goniometer protractor device. The Peyronie's Disease Questionnaire (PDQ)[7] and the International Index of Erectile Function (IIEF) questionnaire[8] were completed at nominal week 36 to assess the physical, psychological, and sexual effects of CCH therapy. The primary efficacy end point was the percentage of change in penile curvature from baseline to nominal week 36. Additional efficacy end points included change from baseline to nominal week 36 in PDQ bother score (PDQ questions 10−15), PD symptom severity score (PDQ questions 1−6), penile pain score (PDQ questions 7−9), and IIEF domain scores (erectile function, questions 1−5 and 15; orgasmic function, questions 9 and 10; sexual desire, questions 11 and 12; intercourse satisfaction, questions 6−8; and overall satisfaction, questions 13 and 14; each IIEF question was rated from 0 ["worst"] to 5 ["best"]).[8] The rate of composite responders, defined as patients who had at least a 20% decrease in penile curvature from baseline and a decrease in PDQ bother score of at least 1 point from baseline or a change from reporting "no sexual activity" to reporting "sexual activity," also was assessed at nominal week 36. Also at week 36, patients were asked to rate the overall change in symptoms and effects of PD on their lives, using the Global Assessment of Peyronie's Disease assessment tool, a seven-point scale that rates improvement from baseline as "much improved" (3) to "much worse" (−3). A global assessment responder was defined as a patient who reported small but important improvement, moderate improvement, or much improvement in the overall global assessment question score. Safety was assessed throughout the study by monitoring adverse events (AEs) and vital signs, clinical laboratory investigations, and assessments of the IIEF erectile function domain.

Statistical Methods

Sample size was not formally calculated; however, the study sponsor stated that a sample of approximately 30 patients would be adequate for this pilot study. The intent-to-treat (ITT) population consisted of all enrolled patients who had at least one injection of CCH. Efficacy analyses were performed in the modified ITT population, which included all enrolled patients who received at least one injection of CCH, had a penile curvature measurement at screening, and at least one post-treatment penile curvature measurement. Primary and other efficacy end points were summarized using descriptive statistics unless otherwise indicated. For the assessment of PDQ domain scores, if answers to more than 50% of the items within the domain were missing, then the domain score was said to be missing; if no more than 50% of the items were missing, then the domain score was calculated as the average of available item scores multiplied by the total number of items in that domain. For the analysis of change variables, missing data were imputed using the last observation carried forward (LOCF) method. Between-group differences in continuous end points (eg, change from baseline) were assessed using analysis of variance with treatment group as a factor. For categorical end points (eg, responder analyses), the odds ratio for response between groups was calculated and the corresponding 95% CI was estimated assuming an asymptotic normal distribution. Calculations were performed using SAS 9.3 (SAS Institute, Cary, NC, USA).

RESULTS

Thirty-six patients were screened; of these, 30 patients were enrolled and randomly assigned to treatment. Overall, the two groups of 15 patients were similar in baseline demographics and disease characteristics (Table 1). Most patients had a penile curvature no greater than 60°. All 30 patients were included in the ITT and modified ITT populations. Most patients in the two treatment groups completed the study (Figure 1). One patient in each treatment group received penile anesthesia before modeling.

Table 1. Patient baseline characteristics

Characteristic	CCH + vacuum + modeling (n = 15)	CCH + vacuum (n = 15)
Age (y), mean (SD)	57.8 (9.4)	57.6 (8.4)
Race, n (%)		
White	15 (100)	14 (93.3)
Asian	0	1 (6.7)
Erectile dysfunction, n (%)	6 (40.0)	5 (33.3)
Trauma to penis reported, n (%)	4 (26.7)	3 (20.0)
Direction of penile curvature, n (%)		
Right lateral	1 (6.7)	0
Dorsal	9 (60.0)	10 (66.7)
Left dorsolateral	5 (33.3)	5 (33.3)
Penile plaques, n (%)		
1	12 (80.0)	14 (93.3)
2	2 (13.3)	1 (6.7)
>2	1 (6.7)	0
Penile curvature (°), mean (SD)	59.0 (15.0)	58.3 (12.2)
Severity of penile curvature, n (%)		
≤60°	10 (66.7)	10 (66.7)
>60°	5 (33.3)	5 (33.3)

CCH = collagenase *Clostridium histolyticum*.

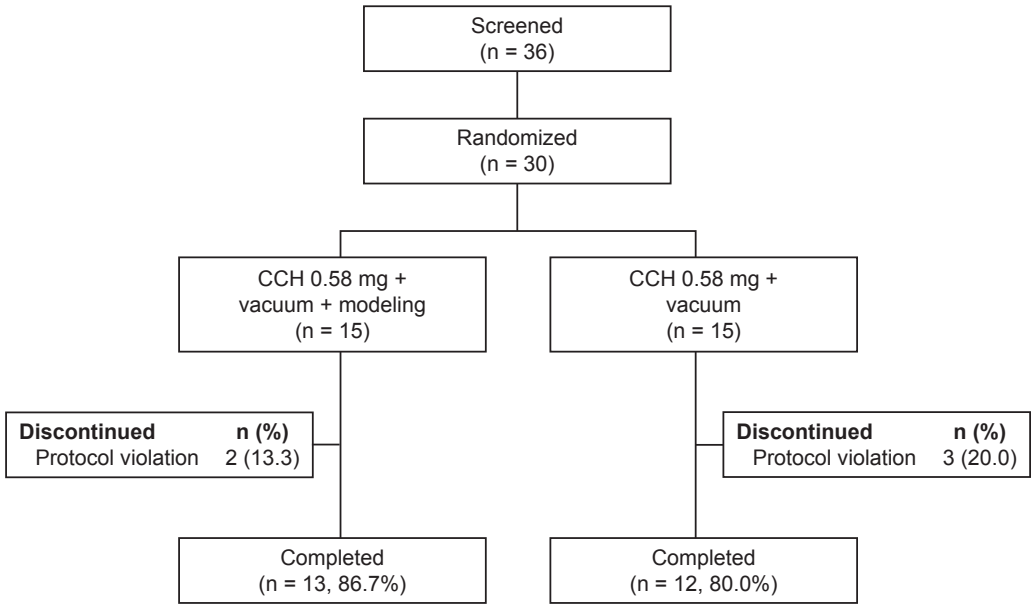

Figure 1. Patient disposition. CCH = collagenase *Clostridium histolyticum*.

Efficacy of CCH Plus Vacuum Therapy

Mean penile curvature at baseline was similar for the two treatment groups. At week 36, a similar improvement in penile curvature was observed in the two groups (mean change from baseline = −23.7° [SD = 10.9] for CCH + vacuum + modeling and −23.3° [SD = 7.2] for CCH + vacuum; between-group difference = −0.3°, 95% CI = −7.3 to 6.6). The mean percentage of decrease from baseline to week 36 also was similar in the two treatment groups (Figure 2).

In addition, improvements in the PDQ scores on the symptom severity and bother domains from baseline to week 36 were observed in the two treatment groups (Table 2). Mean change in PD symptom severity score (LOCF) was numerically larger in the CCH plus vacuum group (mean change = −6.4 [SD = 2.8]) than in the CCH plus vacuum plus modeling group (mean change = −2.2 [SD = 4.4]; treatment difference = 4.1, 95% CI = 0.9 to 7.3). Mean change in PDQ bother domain scores (SD; LOCF) also was numerically greater in the CCH plus vacuum group (−3.8 [SD = 3.0]) compared with the CCH plus vacuum plus modeling group (−2.4 [SD = 2.5]; treatment difference = 1.4, 95% CI = −0.9 to 3.8). Penile pain domain score increased from baseline (indicating greater severity, pain, or bother) in the CCH plus vacuum plus modeling group (mean change from baseline = 0.7 [SD = 3.1], LOCF), but slightly decreased (suggesting improvement) in the CCH plus vacuum group (mean change from baseline = −1.3 [SD = 3.0], LOCF).

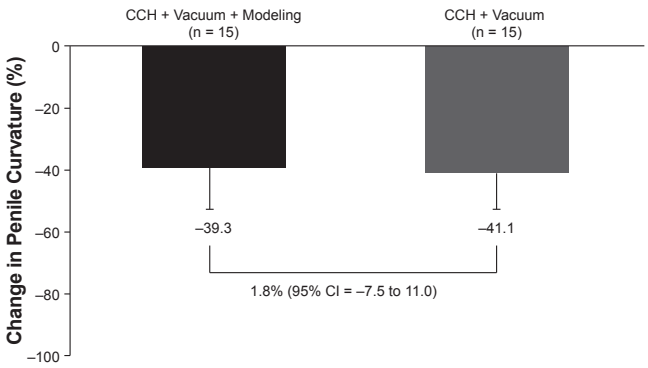

Figure 2. Mean change in penile curvature from baseline to week 36 (last observation carried forward analysis). Between-group difference of 1.8% (95% CI = −7.5 to 11.0). CCH = collagenase *Clostridium histolyticum*.

Mean IIEF erectile function and intercourse satisfaction scores were improved from baseline for patients in the CCH plus vacuum group, whereas slight worsening was observed in the CCH plus vacuum plus modeling group (Table 3).[8] The two groups had an increase in mean IIEF overall satisfaction score (indicating increased satisfaction) from baseline to week 36, although greater improvement was observed in the CCH plus vacuum group. In the group that received CCH plus vacuum therapy with plaque modeling, the mean IIEF overall satisfaction score was 5.9 (SD = 2.5) at baseline and 6.1 (SD = 2.8) at week 36—an increase of 0.3 point (SD = 1.8). In comparison, the baseline satisfaction score in the group that did not undergo modeling was 4.7 (SD = 2.3) compared with 6.8 (SD = 2.5) at week 36—a mean increase of 2.0 points (SD = 2.6; between-group difference = −1.7 points, 95% CI = −3.5 to 0.0).

The percentage of patients who reported a composite response equaled 66.7% in the group that received CCH plus vacuum plus modeling and 84.6% in the group that received CCH plus vacuum without modeling. The odds ratio for composite response in the group that underwent plaque modeling equaled 0.4 (95% CI = 0.1 to 2.3).

Table 2. PDQ domain scores with CCH

PDQ domain score*	CCH + vacuum + modeling (n = 15)	CCH + vacuum (n = 15)	Between-group difference (95% CI)
Penile pain			
Baseline	1.4 (1.7)	4.0 (4.7)	
Week 36	2.7 (3.2)	2.2 (2.4)	
Change from baseline (LOCF)	0.7 (3.1)	−1.3 (3.0)	2.0 (−0.6 to 4.5)
Symptom severity			
Baseline	9.3 (4.7)	12.5 (4.4)	
Week 36	6.9 (3.9)	6.6 (5.4)	
Change from baseline (LOCF)	−2.2 (4.4)	−6.4 (2.8)	4.1 (0.9–7.3)
Bother			
Baseline	6.3 (2.8)	7.8 (3.2)	
Week 36	4.4 (2.9)	4.0 (3.7)	
Change from baseline (LOCF)	−2.4 (2.5)	−3.8 (3.0)	1.4 (−0.9 to 3.8)

CCH = collagenase *Clostridium histolyticum*; LOCF = last observation carried forward; PDQ = Peyronie's Disease Questionnaire.
*Higher scores indicate greater severity, pain, or bother. Data are presented as mean (SD) unless otherwise indicated.

Most patients in the CCH plus vacuum plus modeling group and 92.3% of those in the CCH plus vacuum group reported some degree of improvement (Figure 3). Of note, 53.3% and 69.2%, respectively, reported "moderate" and "much" improvement. The odds ratio for global assessment response (defined as small but important, moderate, or much improvement) at week 36 equaled 0.5 (95% CI = 0.04–6.8).

Safety and Tolerability

In the two groups, all patients reported at least one AE, and most AEs were mild or moderate in intensity. Only one patient, in the group undergoing plaque modeling, reported a severe AE (epilepsy). The most commonly reported AEs in the two groups were penile contusion, swelling, or pain (Table 4). No cases of corporal rupture or penile fracture were reported. Two serious AEs

Table 3. IIEF domain scores with CCH

IIEF domain score* (maximum score possible)[8]	CCH + vacuum + modeling (n = 15)	CCH + vacuum (n = 15)	Between-group difference (95% CI)
Erectile function (30)			
Baseline	25.4 (3.2)	21.9 (7.5)	
Week 36	22.7 (8.8)	23.5 (6.9)	
Change from baseline (LOCF)	−2.8 (10.4)	1.9 (5.5)	−4.7 (−11.4 to 2.1)
Orgasmic function (10)			
Baseline	8.8 (1.9)	8.8 (2.0)	
Week 36	7.8 (3.7)	8.5 (2.4)	
Change from baseline (LOCF)	−1.0 (4.1)	−0.3 (2.6)	−0.7 (−3.5 to 2.2)
Sexual desire (10)			
Baseline	6.6 (2.0)	7.1 (1.6)	
Week 36	6.3 (2.3)	7.2 (1.2)	
Change from baseline (LOCF)	−0.3 (1.6)	−0.1 (1.4)	−0.2 (−1.4 to 1.0)
Intercourse satisfaction (15)			
Baseline	9.5 (3.3)	8.1 (4.0)	
Week 36	8.7 (4.3)	8.5 (4.8)	
Change from baseline (LOCF)	−0.8 (4.5)	0.8 (5.4)	−1.5 (−5.5 to 2.5)
Overall satisfaction (10)			
Baseline	5.9 (2.5)	4.7 (2.3)	
Week 36	6.1 (2.8)	6.8 (2.5)	
Change from baseline (LOCF)	0.3 (1.8)	2.0 (2.6)	−1.7 (−3.5 to 0.0)

Data are presented as mean (SD) unless otherwise indicated.
CCH = collagenase *Clostridium histolyticum*; IIEF = International Index of Erectile Function; LOCF = last observation carried forward.
*Higher scores indicate greater frequency; less difficulty; or higher satisfaction, confidence, or pleasure.[8]

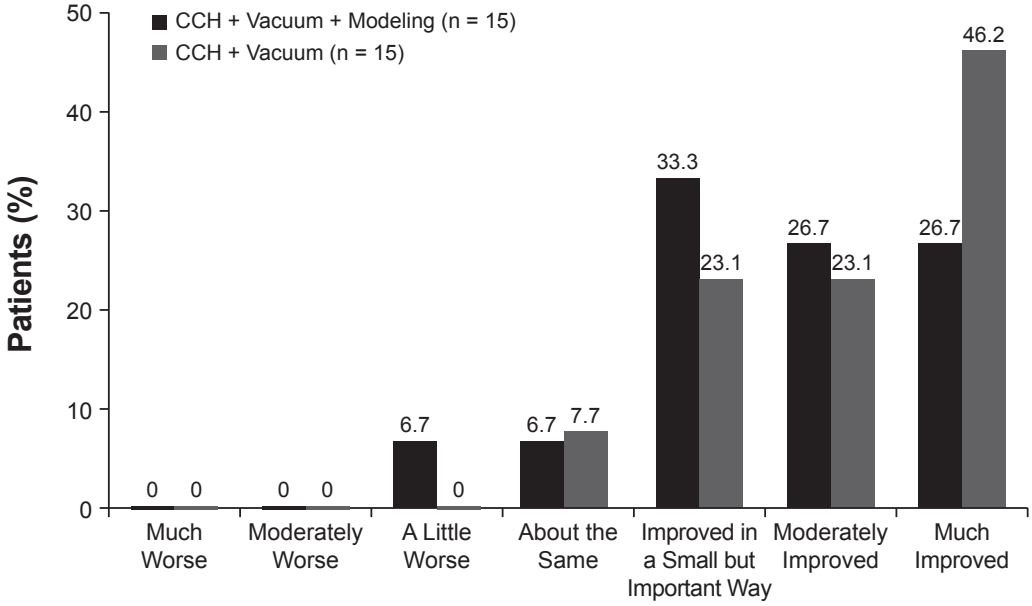

Figure 3. Global Assessment of Peyronie's Disease responses at week 36 (last observation carried forward analysis). CCH = collagenase *Clostridium histolyticum*.

(myocardial ischemia and pericarditis, n = 1 each) were reported in the CCH plus vacuum plus modeling group. The serious AE of pericarditis was considered by investigators to be mild in intensity and occurred after treatment (day 232). Another serious AE, myocardial ischemia of mild intensity, occurred during the second CCH injection of the patient's second treatment cycle (day 55). Neither serious AE required dose adjustment or was considered by the investigator to be related to treatment.

DISCUSSION

Multiple conservative therapies (eg, penile modeling, traction therapy, and vacuum therapy) have been investigated as treatment options for PD based on their ability to facilitate fibrous plaque remodeling and lengthen and/or straighten the penis.[1,9]

Table 4. Most commonly reported AEs*

AE, n (%)	CCH + vacuum + modeling (n = 15)	CCH + vacuum (n = 15)
Any AE	15 (100.0)	15 (100.0)
Penile contusion	13 (86.7)	15 (100.0)
Penile swelling	11 (73.3)	15 (100.0)
Penile pain	8 (53.3)	5 (33.3)
Contusion	3 (20.0)	2 (13.3)
Arthralgia	2 (13.3)	0
Influenza	1 (6.7)	2 (13.3)
Injection-site swelling	1 (6.7)	2 (13.3)
Penile erythema	0	2 (13.3)
URTI	0	3 (20.0)

AE = adverse event; CCH = collagenase *Clostridium histolyticum*; URTI = upper respiratory tract infection.
*At least 10% of patients in either group.

Intralesional injection of CCH is approved for the treatment of PD in adult men with palpable plaque and curvature deformity of at least 30° at therapy initiation. CCH is typically applied in conjunction with penile modeling based on the design of phase 3 trials (in which investigators and patients performed penile modeling for 6 weeks after each CCH treatment cycle).[4] Because penile modeling and vacuum therapy share underlying physiologic mechanisms, the objective of this pilot study was to evaluate a new CCH treatment regimen that included vacuum-pump therapy (with or without modeling) in the management of stable PD in adult men with penile curvature of at least 30°. Treatment with CCH plus vacuum alone or in combination with modeling improved penile curvature by approximately 40% (equivalent to a decrease of approximately 23°). This is slightly greater than the change in penile curvature from baseline (mean improvement from baseline = 17.2°) reported by an open-label study that used vacuum therapy combined with modeling as part of a modified CCH treatment protocol (three CCH injections [0.9 mg] separated by 4 weeks).[10] Furthermore, these results add credence to the findings of a small, uncontrolled, 12-week study that demonstrated improvement in penile curvature with vacuum-pump (Osbon ErecAid, MediPlus, High Wycombe, UK) therapy alone.[6]

In general, PDQ domain scores, including the bother domain, improved with CCH plus vacuum with or without modeling, which reflected the relief of PD symptoms and the potential enhancement of quality of life. In the two treatment groups, the decreases in mean PDQ bother scores were generally comparable with those reported for CCH-treated patients in IMPRESS I and II (mean decrease = 2.8 points).[4] The decrease in bother scores was numerically greater in the CCH plus vacuum group, which might reflect less manipulation of the penis and, hence, less patient

discomfort. However, in the absence of a formal statistical analysis, it is not possible to draw any firm conclusions about the significance of these findings. There was little change in the IIEF overall satisfaction score in the group that underwent plaque modeling (mean = 0.3), whereas the two-point change observed in the group that did undergo plaque modeling was numerically larger than the change reported in the IMPRESS I and II trials[4] and could reflect patient preference for limited penile manipulation in the CCH plus vacuum group. Furthermore, worsening of erectile function domain scores in the CCH plus vacuum plus modeling group (mean change from baseline = −2.8) could be an artifact of penile discomfort attributable to penile modeling. Other changes from baseline in the CCH plus vacuum plus modeling group in IIEF domain scores were small (mean change from baseline = −0.8 to −1.0) and likely attributable to the subjective nature of the questionnaire.

The composite response rate (66.7% and 84.6% for the CCH plus vacuum plus modeling and CCH plus vacuum groups, respectively) and the global assessment response rate (86.7% and 92.3%, respectively) at 36 weeks were numerically higher than the corresponding rates seen with CCH plus modeling at 52 weeks in combined analyses of the IMPRESS I and II trials (60.8% and 46.6% for global assessment responder and composite responder, respectively), which used identical definitions of global assessment and composite response.[4] In addition, in this study, responder rates were higher in the two treatment groups compared with those of patients who received placebo (ie, sham injection and investigator modeling) in the IMPRESS trials (29.5% for global assessment responders and 28.0% for composite responders),[4] suggesting that CCH plus vacuum-pump therapy (alone or in combination with modeling) provided adequate remodeling of the fibrosis plaque. However, the clinical significance of these findings remains to be established in a larger patient population, particularly because composite response and global assessment responder end points included subjective reports of patient improvement, which could have been influenced by factors other than treatment (eg, increased psychologic distress caused by treatment or expectation of improvement [placebo effect]).

The most common AEs in the present study were consistent with those experienced by patients in the IMPRESS trials, in which the most common AEs, which occurred in 45% to 80% of patients who received CCH plus modeling, were penile ecchymosis, penile swelling, and penile pain.[4] The concordance in AE profiles between the present study and the IMPRESS trials suggests that concomitant vacuum-pump therapy does not substantially negatively affect the tolerability of CCH treatment. It is important to note that vacuum therapy was initiated 2 weeks after the last CCH injection to minimize the risk of some AEs, such as ecchymosis and hematoma; earlier initiation of vacuum therapy could increase the risk of some AEs.

The present study has the limitations inherent in pilot trial designs, including a small sample, lack of formal statistical analyses, and limited follow-up duration. In addition, further research is needed to optimize the duration and frequency of vacuum-pump administration and identify characteristics of patients for whom vacuum-pump therapy would be most beneficial. Nevertheless, the results warrant additional studies in larger patient populations to determine whether the combination of CCH and vacuum-pump therapy could be a useful addition to the therapeutic options for the management of PD.

ACKNOWLEDGMENTS

The authors thank Jillian Gee, PhD, Synchrony Medical Communications LLC (West Chester, PA, USA) for providing writing and editorial support under the direction of the authors.

Corresponding Author: David J. Ralph, FRCS, The Institute of Urology, University College London Hospital, 235 Euston Road, London NW1 2BU, UK. Tel: +44-020-3447-9190; Fax: +44-020-3447-9303; E-mail: dralph@andrology.co.uk

Conflicts of Interest: Mr Ralph is a clinical investigator for Auxilium Pharmaceuticals, Inc, and a consultant for Boston Scientific, Coloplast Corp, Auxilium Pharmaceuticals, Inc, and Sobi, Inc. Dr Abdel Raheem is a clinical investigator for Auxilium Pharmaceuticals, Inc, and a consultant for Sobi, Inc. Dr Liu is an employee of Endo Pharmaceuticals, Inc.

Funding: This study was funded by Endo Pharmaceuticals, Inc. Although Endo Pharmaceuticals, Inc was involved in the data analysis, interpretation, and fact checking of information, the content of the report, the ultimate interpretation, and the decision to submit for publication were determined by the authors independently.

STATEMENT OF AUTHORSHIP

Category 1

(a) Conception and Design
David J. Ralph; Amr Abdel Raheem

(b) Acquisition of Data
David J. Ralph; Amr Abdel Raheem

(c) Analysis and Interpretation of Data
David J. Ralph; Amr Abdel Raheem; Genzhou Liu

Category 2

(a) Drafting the Article
David J. Ralph; Amr Abdel Raheem; Genzhou Liu

(b) Revising It for Intellectual Content
David J. Ralph; Amr Abdel Raheem; Genzhou Liu

Category 3

(a) Final Approval of the Completed Article
David J. Ralph; Amr Abdel Raheem; Genzhou Liu

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