Clinical Evaluation of Treatment of Peyronie’s Disease With Collagenase Clostridium Histolyticum: Analysis of Penile Curvature Deformity by Duration of Disease and Plaque Calcification

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ABSTRACT

Introduction and Objective: Three phase 3 studies have been conducted to examine the safety and efficacy of collagenase clostridium histolyticum (CCH) in subjects with Peyronie’s disease (PD). The purpose of CCH is to improve penile curvature deformity from baseline to end of study was analyzed by the subjects’ duration of disease or degree of plaque calcification.

Methods: All subjects within the study (2 randomised, double-blind, placebo-controlled, pivotal, phase 3 clinical trials of 52 weeks duration (IMPRESS I and II) and one open-label, phase 3 clinical trial of 72 weeks duration. The primary purpose of the open-label trial was to add additional subjects to obtain additional safety information for a more complete evaluation of safety. Eligible Subjects: Male subjects in good health, aged ≥18 years, with stable disease, and symptoms of PD for at least 12 months before the first dose. Limited use for treatment benefit has been found with minimally invasive treatment options as most clinical studies are small and not well controlled. Surgical correction is recommended when the penile curvature deformity impedes adequate sexual penetration or there is associated erectile dysfunction that does not respond to medical treatment. The progression of PD may eventually lead to calcification but the mechanism of this process is also poorly understood. There is evidence that the fibrotic plaque tissue contains progenitor cells that in culture can differentiate into osteogenic cells that may eventually lead to ossification through paracrine modulation. Myofibroblasts are shown to originate from intermediate progenitors in certain organs and play a critical role in the development of tissue fibrosis.

In patients with PD, myofibroblasts disperse by apoptosis after the injury is repaired but are found in abundance in PD plaque in men, suggesting that plaque may continue to produce collagen and contribute to the progression of PD plaque.

As an active process, it would be expected that the duration of disease would show a relationship with degree of calcification. However, a recent study of CCH treatment indicated that the degree of calcification may affect the prognosis with treatment. Ultrasound appears to be superior to all other methods for the detection of calcification.

Method: In normal wound healing, myofibroblasts disappear by apoptosis after the repair is complete. In this study population, duration of disease or degree of calcification was not related to the presence of calcification.

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RESULTS

- The mean age of the population was 57.4 years (range 23-84), predominantly white, and mean penile curvature deformity at baseline was 50° (43.23% of subjects), 60°-70° (31.22% of subjects), and >70° (25.55% of subjects). Mean duration of disease was 3.8 years (range 0.8-35.5).
- Change in mean penile curvature deformity at Weeks 36/52 in CCH-treated subjects (n=775) were stratified by duration of disease as shown in Figure 1.
- The duration of disease had no relationship to reduction in penile curvature deformity at baseline is shown in Figure 3.
- Change in mean penile curvature deformity at baseline is shown in Figure 3.

CONCLUSIONS

- Treatment with CCH resulted in improvements in penile curvature deformity, regardless of duration of disease or degree of plaque calcification. Some small differences were noted within the subgroups, but they were not expected to be clinically meaningful.
- In this study population, duration of disease had no clinical meaningful relationship to plaque consistency or degree of calcification.
- Although there was no association between duration of disease and degree of calcification, further exploration is needed to develop a better understanding of the relationship of duration of disease and degree of plaque calcification. In this study, it was acceptable for subjects to have noncontiguous calcification and calcification if it did not interfere with the injection of CCH. Subjects who had plaques with calcification that interfered with the injection were excluded. Also, the study was not designed to examine the natural progression of plaque calcification over time.

INTRODUCTION

- Peyronie’s disease (PD) is a localized, fibrotic connective tissue disorder that occurs at the site of the pathological deposition of collagen (predominantly Type I and III) in the tunica albuginea of the corpus cavernosum. The clinical presentation may include a palpable lump or palpable bump or modulus along the penile shaft, complaints of penile pain, sexual dysfunction, and diminished quality of life. The cause of PD is not completely understood. However, it is currently referred to as a wound healing disorder because after trauma to the penis the release of cytokines can activate fibroblast proliferation that may lead to collagen deposition and formation of PD plaque. The progression of PD plaque from trauma to the erectile penis is generally accepted. Limitation for treatment benefit has been found with minimally invasive treatment options as most clinical studies are small and not well controlled. Surgical correction is recommended when the penile curvature deformity impedes adequate sexual penetration or there is associated erectile dysfunction that does not respond to medical treatment. The progression of PD may eventually lead to calcification but the mechanism of this process is also poorly understood. There is evidence that the fibrotic plaque tissue contains progenitor cells that in culture can differentiate into osteogenic cells that may eventually lead to ossification through paracrine modulation. Myofibroblasts are shown to originate from intermediate progenitors in certain organs and play a critical role in the development of tissue fibrosis.

In patients with PD, myofibroblasts disperse by apoptosis after the injury is repaired but are found in abundance in PD plaque in men, suggesting that plaque may continue to produce collagen and contribute to the progression of PD plaque. As an active process, it would be expected that the duration of disease would show a relationship with degree of calcification. However, a recent study of CCH treatment indicated that the degree of calcification may affect the prognosis with treatment. Ultrasound appears to be superior to all other methods for the detection of calcification.

REFERENCES

7. XAPLD (collagenase clostridium histolyticum) study group; Amodeo D, Malvern, PA: Auxilium Pharmaceuticals, Inc.; 2012.

DISCLOSURES

Speaker, clinical investigator, advisor for Auxilium (6); investigator for Angiome, Auxilium, Amgen, Astra, Attelios, Biogen, CBT, Celgene, Cephalon, Genentech, Genzyme, Boehringer, Honey, Orphanet Research, Orphanet Therapeutics, Medizinische Leon, Novartis, Ortho, OSOT, PPD, Regeneron, Repligen, Roche, Sano, Schering-Plough, Siemens, Domen, Novartis, AMMG, Glass, Medication and Attelios, consultant for Brandenberg, Bayer, BioArts, Biogen, Boehringer, Edwards, Genzyme, Biogen, Genentech, and Orphanet Research.

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