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A PSA-ACTIVATED PROTOXIN (PRX302) ADMINISTERED TRANSPERINEALLY TO MEN WITH BPH IS WELL TOLERATED AND INDUCES REDUCTION IN PROSTATE VOLUME AND SYMPTOMATIC RELIEF.

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INTRODUCTION AND OBJECTIVES: The use of PSA-activated therapy for the treatment of BPH is a novel approach. PRX302 is a protoxin that was modified to be activated by PSA. In a Phase I study, transperineal administration of PRX302 to men with symptomatic BPH was well tolerated and provided symptomatic relief, evidenced by sustained decreases in IPSS and QOL scores. Here we report results at 90 days post-treatment of a Phase II study of transperineal administration of increasing volumes of PRX302 in patients with symptomatic BPH.

METHODS: A total of 18 patients with a mean age of 66.1 yrs and a mean prostate volume of 49.3 cc received transperineal injections of PRX302 under TRUS guidance. Three cohorts of 6 patients each were treated at a fixed concentration of 3 µg/mL and at volumes equivalent to 10%, 20% and 30% of prostate volume. PRX302 was administered through a single injection into the transition zone of each lobe of the prostate with 3 deposits of equal volume made along the needle track. Patients were evaluated using IPSS, QOL score, prostate volume and uroflowmetry (Qmax).

RESULTS: To date all patients have completed the Day 30 visit and 12 have completed the 3 months active study period. An overall analysis, irrespective of cohort assignment, showed a decrease in mean IPSS from 20.2±4.7 at screening to 13.1±5.1 at 1 month and 12.2±7.2 at 3 months post-treatment ($p<0.01$). QOL scores decreased from a mean of 4.5±1.1 at screening to 2.7±1.5 at 1 month and 2.6±1.3 at 3 months post-treatment ($p<0.01$). Mean prostate volume also decreased by 22% and 18%, at 1 and 3 months post-treatment, respectively. In addition, mean Qmax increased from 10.8±3.2 mL/sec at screening to 12.0±5.0 and 12.0±4.5 mL/sec, at 1 and 3 months following treatment. Results to date indicate that increasing volumes of PRX302 are well tolerated. No serious adverse events (SAEs) or Grade 3 or higher adverse events (AEs) were seen with most AEs being mild to moderate and transient. In addition, no effect on erectile function was observed with similar IIEF scores reported pre and post-treatment.

CONCLUSIONS: Transperineal administration of increasing volumes of PRX302 is well tolerated. Symptomatic improvements in the form of decreased IPSS and QOL scores were observed along with reduction in prostate volume and increase in maximal flow rates. PRX302 appears to provide symptomatic relief and might constitute a promising treatment for patients with BPH.

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HISTOTRIPSY ABLATION OF THE PROSTATE: EVALUATION OF HISTOPATHOLOGY, SAFETY, AND TOLERABILITY IN A CHRONIC CANINE MODEL

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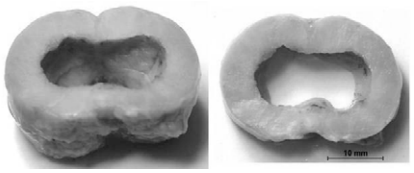
INTRODUCTION AND OBJECTIVES: Histotripsy is an extracorporeal ablative technology that utilizes microsecond pulses of intense ultrasound (<1% duty cycle) to produce non-thermal, mechanical fractionation of targeted tissue. We have previously demonstrated the feasibility of histotripsy prostate ablation. In this study we sought to assess the chronic tissue response, tolerability and safety of histotripsy in a chronic in vivo canine model.

METHODS: Five acute and thirteen chronic canine subjects were anesthetized and treated with histotripsy targeting the prostatic urethra and adjacent glandular tissue. Pulses consisting of 3 cycle bursts of 750 kHz ultrasound at a repetition rate of 300 Hz were delivered from a highly focused 15 cm aperture array. This therapy array was attached to a computerized 3-axis positioning system for trans-abdominal targeting of the prostate. Prostates were harvested at 0, 7, 28, or 56 days after treatment. Blood and urine samples were collected before histotripsy, one day following treatment, and at harvest. Pain was assessed daily using a veterinary pain scale.

RESULTS: Transrectal ultrasound imaging provided accurate targeting and real-time monitoring of histotripsy treatment. Consistent mechanical tissue fractionation and debulking of prostate tissue was seen acutely and at delayed time points without collateral injury. Urothelialization of the treatment cavity was apparent 28 days after treatment. Canine subjects tolerated histotripsy with minimal hematuria or discomfort. Only mild transient lab abnormalities were noted.

CONCLUSIONS: Histotripsy is a promising non-invasive therapy for prostate tissue fractionation and debulking that appears safe and well tolerated without systemic side effects in the canine model.



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LIGHT-ACTIVATED DRUG THERAPY FOR BPH

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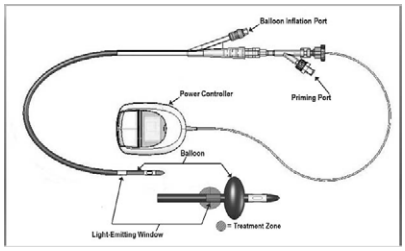
INTRODUCTION AND OBJECTIVES: The light-activated drug therapy, Litx™, is a disposable system that uses light-emitting diodes (LEDs) to activate LS11® (talaporfin sodium), producing singlet oxygen in exposed tissue and leading to localized cell death. Preclinical and clinical studies were designed to assess the safety and potential effectiveness of Litx™ in BPH.

METHODS: We conducted 6-month studies of Litx™ in 57 beagles (age~18 mo) followed by a Phase I light-dose escalation study in 6 men with BPH refractory to drug therapy (50-80 y.o., IPSS > 12, Qmax 50 cc). Treatments utilized a single-use Foley catheter incorporating a 10 mm-long array of LEDs (664 +/-5 nm). In dogs, under general anesthesia the catheter was placed; LS11 at 25 mg/kg was administered IV; and the Litx™ device was activated via a remote power source (50 or 70 J/cm). In man, the catheter was placed using only lidocaine intraurethrally; LS11 at 1mg/kg was administered IV; and the Litx™ device was activated (50 or 70 J/cm). All men were treated in an office setting. Animal protocols were approved by IACUUC, and the clinical protocol was approved by Western IRB.

_____Litx™ device components_____



RESULTS: IN DOGS, at 2- or 7-day necropsy a dose-dependent 'kill zone' up to 20-25% of PV surrounding the urethra was observed. The urothelium was relatively spared, and the treatment effect was confined to prostate. No urinary retention was seen. Healing of lesions was grossly apparent after 30 days. IN MAN, the treatment was painless. All patients