The Safety and Efficacy of Li-ESWT in 604 patients for Erectile Dysfunction: Summary of Current and Evolving Evidence

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INTRODUCTION AND OBJECTIVES

Low intensity shock wave therapy (Li-ESWT) is currently approved in over 20 countries and available at over 200 clinics worldwide. A US multicenter study has been completed and the data are currently under FDA review. Herein we provide an overview of the clinical experience to date on the safety and efficacy of Li-ESWT for the treatment of erectile dysfunction. Studies were conducted in men with ED considered responders and in men considered poor responders to PDE5i. We report pooled data from 5 randomized, placebo-controlled studies (USA, Israel, Greece and India) and 3 single-arm open label studies (Israel, Japan). Li-ESWT for ED has been recently included in the European Association of Urology guideline 2013 for male sexual dysfunction

METHODS:

The database included men (N=604) using the same treatment protocol with Li-ESWT (ED1000 Medispec applicator; Active Rx N=440; Sham Rx N=164).; Li-ESWT was applied to the corpora 2X weekly for 3 weeks and repeated after a 3 week rest period for a total of 12 Rx sessions. Changes in IIEF-EF domain were assessed at baseline and at mid-treatment; 1 month (FU1), 3 months (3M), 6 months (FU2) and 12 (FU3) post last treatment. Objective measurements of efficacy were assessed by various measures including penile US Doppler (Greece, penile triplex), Flow Mediated Dilation (FMD, Israel) and nocturnal penile tumescence (NPT, USA). Incidence and severity of adverse events were recorded.

RESULTS

Results of pooled data revealed that 56.4%, 66.5%, 63.2% and 62.1% of the subjects achieved a minimally clinical important difference (MCID) in their –IIEF-EF score from baseline at midterm, FU1, FU2 and FU3 respectively. The mean change in IIEF-EF from baseline was 5.4, 7.4, 6.4 and 5.9 points at midterm, FU1, FU2 and FU3 respectively. Li-ESWT applied via the ED-1000 was well tolerated; reported AEs were mild and resolved spontaneously. Results from selected studies in which objective measures were assessed are presented in table 1.

Table 1 Results from selected studies in which objective measures were assessed:

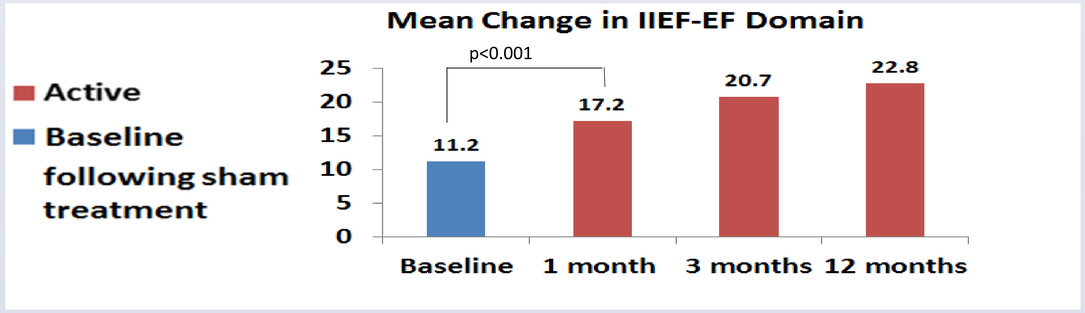
Country	USA	Greece	Israel-		
	RCT	RCT	RCT 1	*Group D	**RCT2
Response to PDE5i prior to Li-ESWT	Responders	Responders	Responders	Responders	Poor responders
***MCID II-EF EF-EF domain	62% vs. 37.5% in treatment vs. placebo group, p=0.025	58.6% vs.12.5% in treatment vs. placebo group, p=0.003	49.3% vs. 9.1% in treatment vs. placebo group, p<0.01	45.8% vs. 12.5% in treatment vs. placebo group, p=0.021	40.5% vs. 0% in treatment vs. placebo group, p=0.001
IIEF-EF mean change from baseline	6.1 vs.2.5 points in treatment vs. placebo group, p=0.02	4.6 vs.1.4 points in treatment vs. placebo group, p<0.001	5.3 vs. 0.2 in treatment vs. placebo group, p<0.001	5.5 vs. -0.1 points in treatment vs. placebo group, p<0.001	5.4 vs. 0.1 points in treatment vs. placebo group, p<0.001
US Doppler	NA	PSV increased by 4.5 vs. 0.6 cm/sec in treatment vs. placebo, p<0.001	NA	NA	NA
FMD	NA	NA	Mean AUC difference, treatment vs. placebo, 361.3 p=0.002	Mean AUC difference, treatment vs. placebo, 316.9 p=0.002	Mean AUC difference, treatment vs. placebo, 276.2 p=0.001
NPT	Mean difference treatment vs. placebo, 0.52 p=0.016	NA	NA	NA	NA
Population	103 pt. (treatment-84, placebo-40)	46 pt. (treatment-31, placebo-15)	89 pt. (treatment-59, placebo-30)	24 pt.	55 pt. (treatment- 37, placebo-18)
*Group D	Subjects from the placebo group of the RCT study, who did not demonstrated significant improvement in their IIEF-EF domain score, received an additional treatment course with an active shockwave applicator. The treatment protocol those subjects received was identical to the original study protocol.				
**RCT	Subjects that were poor responders to PDE5i prior to Li-ESWT, were allowed PDE5i use at baseline and following last treatment until FU1 assessment (all pt. achieved erection hardness score ≤2 at baseline, and EHS≥3 in 62% at FU1 . Population pilot study included).				
***MCID (ROSEN)	Success define as: an increase in the IIEF-EF Domain score ≥ 2 points from baseline for mild ED, ≥ 5 points for moderate ED, and ≥ 7 points for severe ED,. ED Severity define as : Mild ED – IIEF-EF score 17-22 ,Moderate ED –IIEF-EF score 11-16, Severe ED –IIEF-EF score 0-10				

ED Severity level according to IIEF-EF domain	Mid treatment evaluation**		1st month post last treatment		6th months post last treatment		12th months post last treatment	
	N	%	N	%	N	%	N	%
Total Mild	50	60.0	51	70.6	49	69.4	49	75.5
Total Moderate	113	55.8	113	66.4	113	64.6	113	58.4
Total Severe	117	55.6	117	65.0	115	59.1	115	60.0
Total all	280	56.4	281	66.5	277	63.2	277	62.1

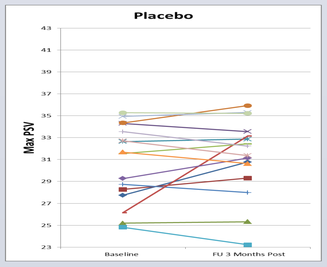
Patient Success according to IIEF-EF domain Minimal clinically important differences *(Rosen Criteria)- PDE5i responders patients: USA, Greece, Israel and India Population

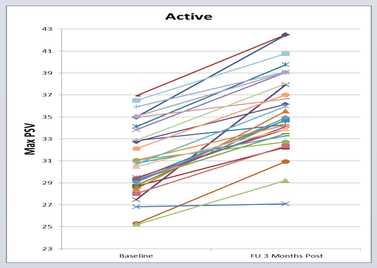
*Rosen RC, Allen KR, Ni X, Araujo AB. Minimal clinically important differences in the erectile function domain of the International Index of Erectile Function scale. European urology. Nov 2011;60(5):1010-1016.
**Mid treatment evaluation following 6 treatment sessions

PDE5i following LI ESWT - change in Erection Hardness Score in PDE5i poor responders prior to ESWT
29 pt. participated in the feasibility study
37 pt. participated in the in the RCT



Patients who received active treatment following sham treatment ("Group D")- in patients who responded to PDE5i prior to ESWT





Doppler results – Greece

Individual Plots Describing Maximal Peak Systolic Velocity in patients who responded to PDE5i prior to ESWT

CONCLUSIONS

In these pooled data analyses, Li-ESWT was demonstrated to be safe and effective for the treatment of ED in men considered responders as well as non-responders to PDE5i therapy. Li-ESWT was well tolerated, adverse events were mild, self-limited and resolved spontaneously. These results support the role of Li-ESWT in the management of men with ED.

References

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