The Safety and Efficacy of LI-ESWT in 604 patients for Erectile Dysfunction with ED 1000

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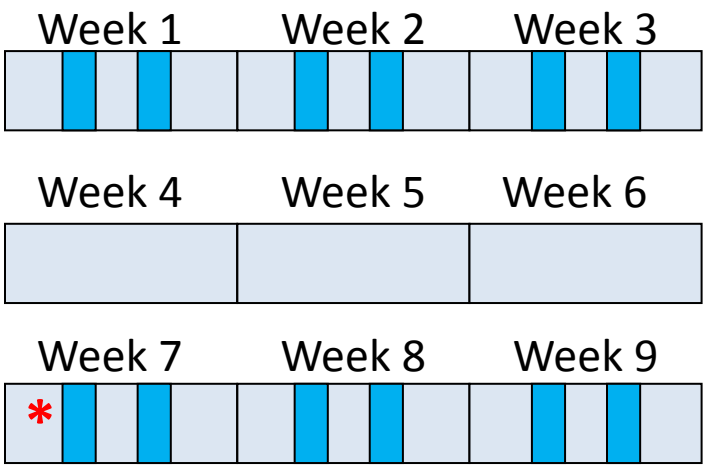
In the USA: ED 1000 is limited by Federal law to investigational use.

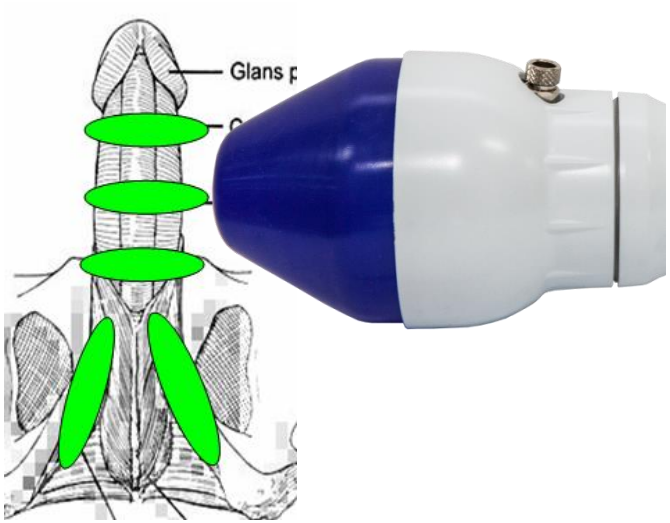
LI-ESWT- Painless, No Anesthesia is required, Quiet
App. 10 % of ESWL-Bar pressure

AUA Annual Meeting
May 15 – 19, 2015
New Orleans, LA, USA

Treatment Protocol and Method



* **Mid treatment evaluation**



Standard protocol:

- 12 treatment sessions
  - i. Twice weekly X 3 weeks
  - ii. 3 weeks rest (mid treatment evaluation- following 6 treatment sessions*)
  - iii. Twice weekly X 3 weeks
- 5 treatment areas along the corpora
- 300 shocks per area at 0.09 mj/mm^2
- 1,500 shocks per treatment
- Total 18,000 shocks (mid treatment evaluation following 9000 shocks)

Total Treatment Time per session : 15 minutes

Safety Results

480 patients who participated in 8 studies (US, Israel, Greece, India and Japan) excludes sham treated patients

- 2 patients have experienced a tingling sensation at the tip of the penis during treatment (0.4%)
- 1 patient has experienced the sensation of genital burning (0.2%)
- 1 patient has experienced application site hypersensitivity (0.2%)
- 2 patients have developed a skin rash due to sensitivity to the application gel (0.4%)*

All the above AEs were self-limited and self-resolved

Treatment with the ED-1000 was well tolerated, reported AES were mild and infrequent and support a favorable safety profile

*One patient from the sham group developed skin rash due to sensitivity to the application gel

Efficacy assessments

Subjective measures :

IIEF-EF domain questionnaire – Data from USA, Israel, Greece and India

Objective measures :

US Doppler - Data from Greece

Flow Mediated Dilation- FMD - Data from Israel

Nocturnal Penile Tumescence - Data from USA

Mean Changes in IIEF-EF Domain From Baseline – in PDE5i Responders pt. (LI-ESWT monotherapy)

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	Mean	N	Mean	N	Mean	N	Mean
Total Mild	52	2.8	52	3.9	52	3.6	52	4.3
Total Moderate	113	4.9	113	6.8	113	5.8	113	5.4
Total Severe	117	7.0	117	9.6	117	8.3	117	7.1
Total All	282	5.4	282	7.4	282	6.4	282	5.9

USA, Greece ,Israel , India Population

* Mid treatment evaluation following 6 treatment sessions

Patient Success according to IIEF-EF domain

Minimal clinically important differences * (Rosen Criteria)

PDE5i responders pt.- USA, Greece, Israel and India Population

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

* Mid treatment evaluation following 6 treatment sessions

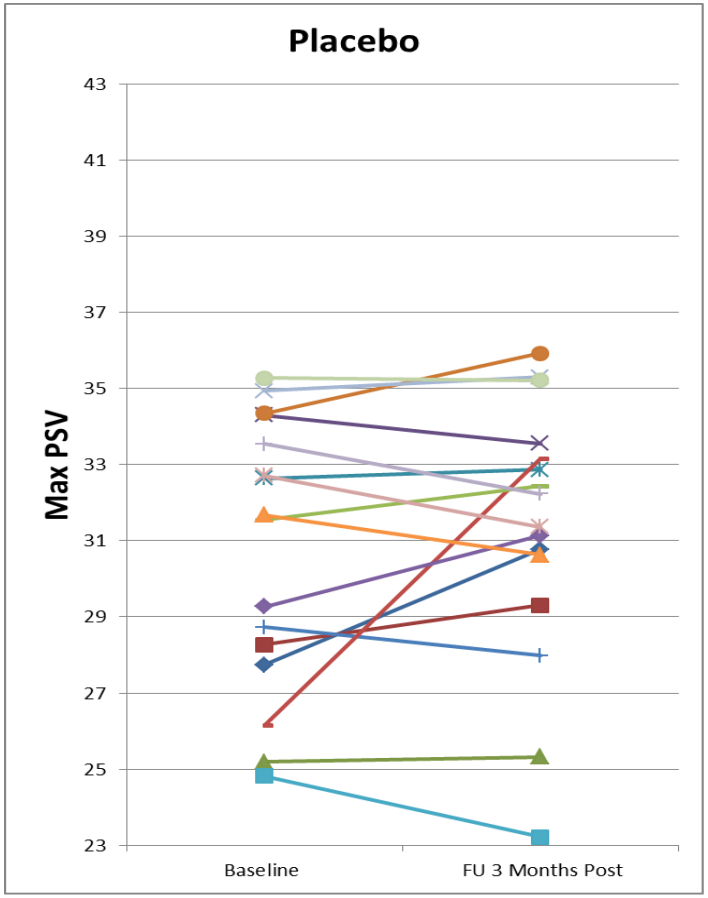
* Rosen RC, Allen KR, Ni X, Araujo AB. Minimal clinically important differences in the erectile function domain of the International Index of Erectile Function scale. *European urology.* Nov 2011;60(5):1010-1016.

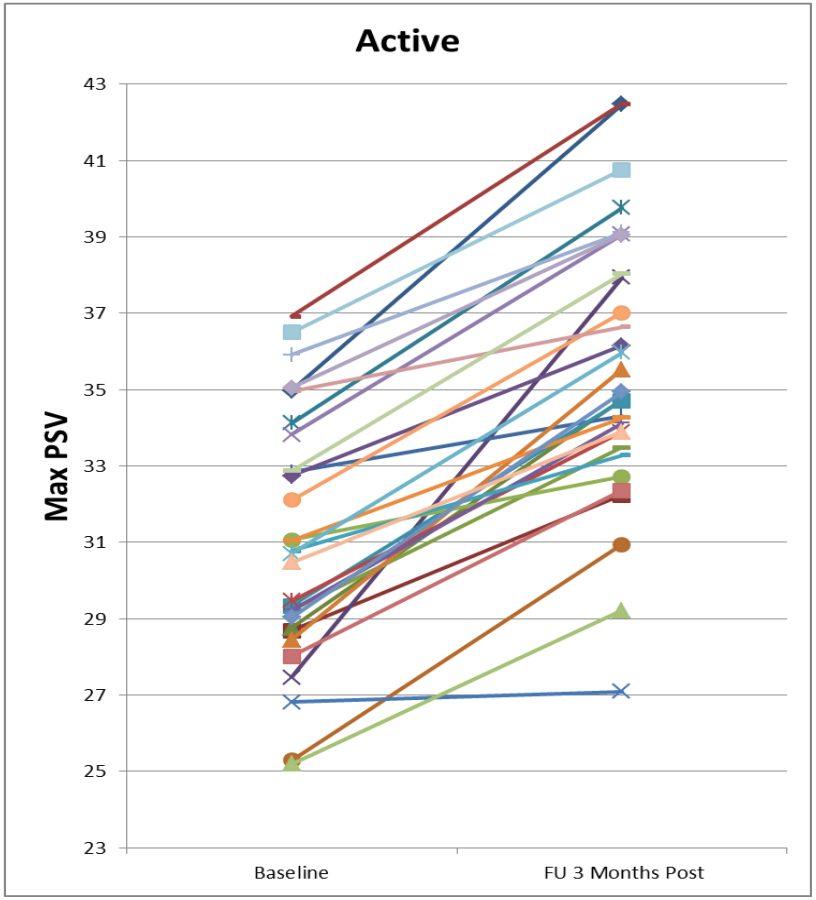
Subjective vs. Objective Measures in Individual Studies

Country	USA	Greece	Israel		
	RCT	**RCT**	**RCT 1**	***Group D**	****RCT2**
Response to PDE5i prior to Li-ESWT	Yes	Yes	Yes	Yes	No
***MCID II-EF EF-EF domain** Treatment vs. placebo group	62% vs. 37.5% p=0.025	58.6% vs. 12.5% p=0.003	49.3% vs. 9.1% p<0.01	45.8% vs. 12.5% p=0.021	40.5% vs. 0% p=0.001
IIEF-EF change from baseline (Treatment vs. placebo group)	6.1 vs. 2.5 points p=0.02	4.6 vs.1.4 points p<0.001	5.3 vs. 0.2 points p<0.001	5.5 vs. -0.1 points p<0.001	5.4 vs. 0.1 points p<0.001
Self objective measures	**NPT**	**US Doppler**	**FMD**	**FMD**	**FMD**
(Treatment vs. placebo group)	Mean difference 0.52 p=0.016	PSV increased by 4.5 vs. 0.6 cm/sec , p<0.001	Mean AUC difference, 361.3 p=0.002	Mean AUC difference, 316.9 p=0.002	Mean AUC difference, 276.2 p=0.001
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

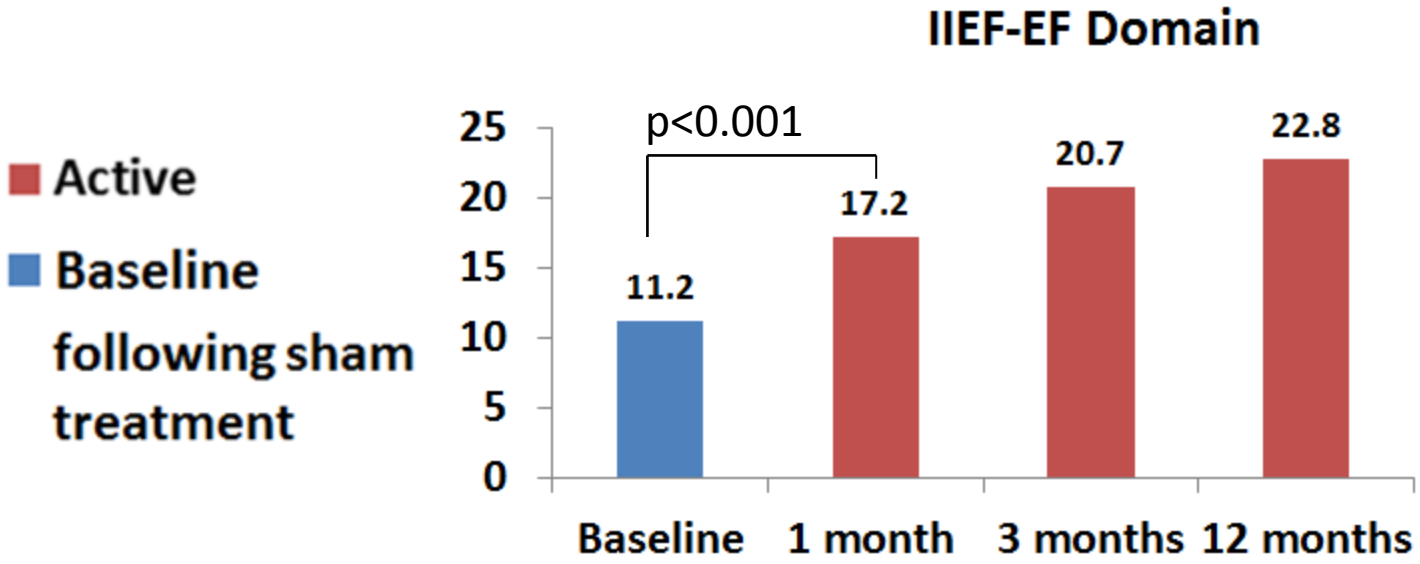
Doppler results - Greece

Individual Plots Describing Maximal Peak Systolic Velocity





Patients who received active treatment following sham treatment ("Group D")



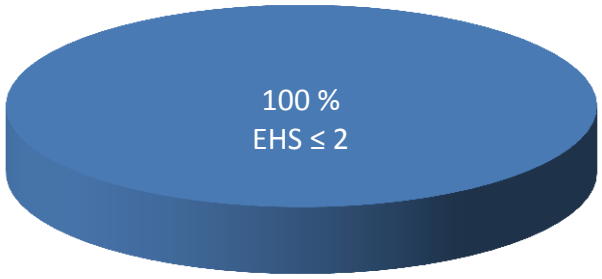
- 25 out of 30 pt. originally participated in the study in the sham treatment group
- 80% of the original sham treatment group received active treatment following FU assessments

Israel PDE5i Non-Responders Converted to Responders

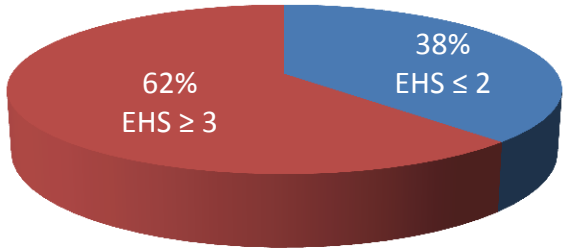
PDE5i following LI ESWT - change in Erection Hardness Score -

66 patients

EHS before treatment



EHS after treatment



29 pt. participated in the feasibility study
37 pt. participated in the in the RCT

Take Home Messages

- LI-ESWT is safe, effective and well tolerated in the treatment of ED
- The standard 12 treatment protocol is effective in both PDE5i responders and in PDE5i poor responders with long term durability.
- Improvement demonstrated in IIEF-EF at mid-treatment evaluation (after 6 treatments) across all severity levels of ED.
- Further Dose Response studies are planned to define the optimal treatment protocol for select populations.

List of publications:

1. Vardi Y, Appel B, Jacob G, Massarwi O, Gruenwald I. Can low-intensity extracorporeal shockwave therapy improve erectile function? A 6-month follow-up pilot study in patients with organic erectile dysfunction. *European urology.* 2010;58(20451317):243-248.

2. Vardi Y, Appel B, Kilchevsky A, Gruenwald I. Does low intensity extracorporeal shock wave therapy have a physiological effect on erectile function? Short-term results of a randomized, double-blind, sham controlled study. *The Journal of urology.* May 2012;187(5):1769-1775.

3. Gruenwald I, Appel B, Vardi Y. Low-intensity extracorporeal shock wave therapy--a novel effective treatment for erectile dysfunction in severe ED patients who respond poorly to PDE5 inhibitor therapy. *The journal of sexual medicine.* 2012;9(22008059):259-264.

4. Gruenwald I, Appel B, Kitrey ND, Vardi Y. Shockwave treatment of erectile dysfunction. *Therapeutic advances in urology.* Apr 2013;5(2):95-99.

5. Srini VS, Reddy RK, Shultz T, Denes B. Low intensity extracorporeal shockwave therapy for erectile dysfunction: a study in an Indian population. *The Canadian journal of urology.* Feb 2015;22(1):7614-7622.

Clinical Results and Population

Pooled data analysis

USA FDA Study, Greece, Israel India and Japan
10 studies assessing safety and efficacy

Country	# Pt.	Mean age	Duration of ED
USA	145	56.3	5
Greece	46	53.7	5.5
Israel	**221	58.8	5.2
India	135	40.1	NA
Japan	57	64	3
***Total**	**604**	**54**	**4.9**

European Association of Urology

Guidelines on Male Sexual Dysfunction:

Erectile dysfunction and premature ejaculation

E. Wespes (chair), I. Eardley, F. Giuliano, D. Hatzichristou,
K. Hatzimouratidis (vice-chair), I. Moncada, A. Salonia, Y. Vardi

Currently Approved and available in more than 50 countries and included in the European guidelines

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