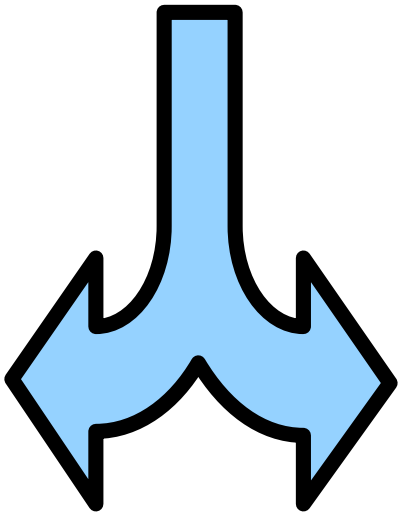
Terapia della Disfunzione Erettile: cosa c'è di nuovo?

Dr Pier Andrea Della Camera

Dr Pier Andrea Della Camera

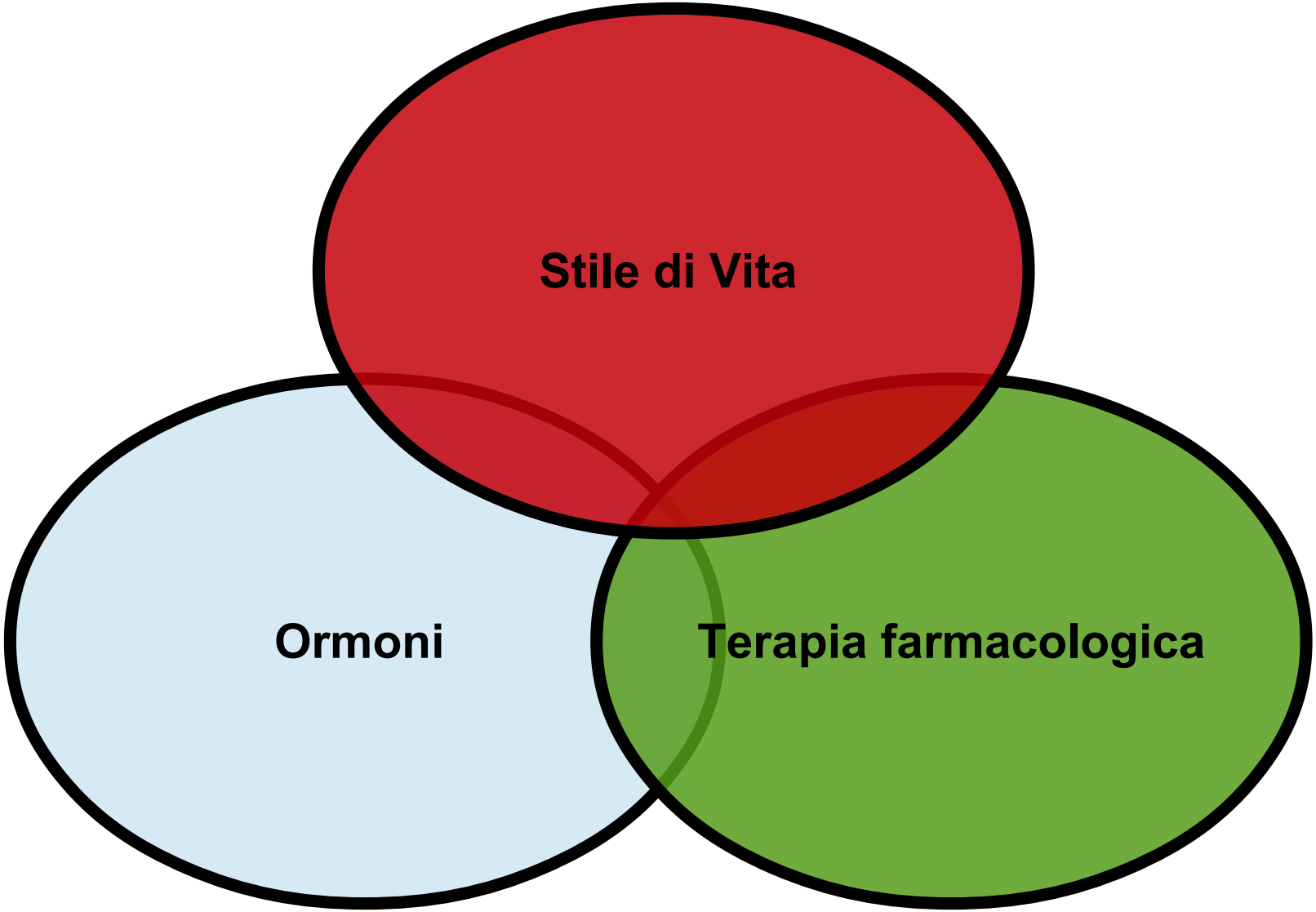
- Fellow of European Board of Urology (Febu)
- International College of Robotic Surgeons
- Dipoma Ircad, Universita' di Strasburgo Laparoscopia Urologica
- Diploma Eropean Basic Laparoscopic Skill (EBLUS)
- Diploma European Stone Treatment (ESt 1)
- Diploma Ecografia Generale, Siumb (Societa' Italiana di Ultrasonografia in Medicina e biologia)
- Diploma Chirurgia Andrologica Nasa / Nasa Evo
- Andrologo Certificato S.I.A. (Societa Italiana di Andrologia)

La disfunzione erettile è l'incapacità di ottenere o mantenere un'erezione soddisfacente durante un rapporto sessuale



Disfunzione erettile semplice

Disfunzione erettile post prostatectomia


Stile di Vita
Ormoni
Terapia farmacologica

Nuovi pde-5 orali

-Avanafil (Speedra)

-Nuovi pde-5 orosolubili (Siler)

Nuova formulazione prostaglandine

-Vitaros

Onde d'urto nella D.E. (Li-eswt)

Avanafil

ARCH ITAL UROL ANDROL
FOUNDED IN 1924
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A survey on the experience of 136 Italian urologists in the treatment of erectile dysfunction with PDE5 inhibitors and recommendations for the use of Avanafil in the clinical practice.

Mirone V[1], Fusco F, Parazzini F, Zucchi A.

RESULTS: The following recommendations on the use of Avanafil were issued: 1) In patients who are candidates for the use of Avanafil, it is advisable to use the 200-mg dose from the first administration; 2) When used at the highest dose (200 mg), Avanafil shows a favourable tolerability profile with an efficacy similar to that of other agents; 3) The patient should be instructed to take Avanafil on an empty stomach, i.e., 30-45 minutes before or 2 hours after a meal; 4) The efficacy window of Avanafil is between 30 minutes and 6 hours after dosing, which qualifies this molecule as a new drug with an intermediate duration of action; 5) Avanafil at a dose of 50-100 mg/day may be a therapeutic option in chronic rehabilitation.

SIA
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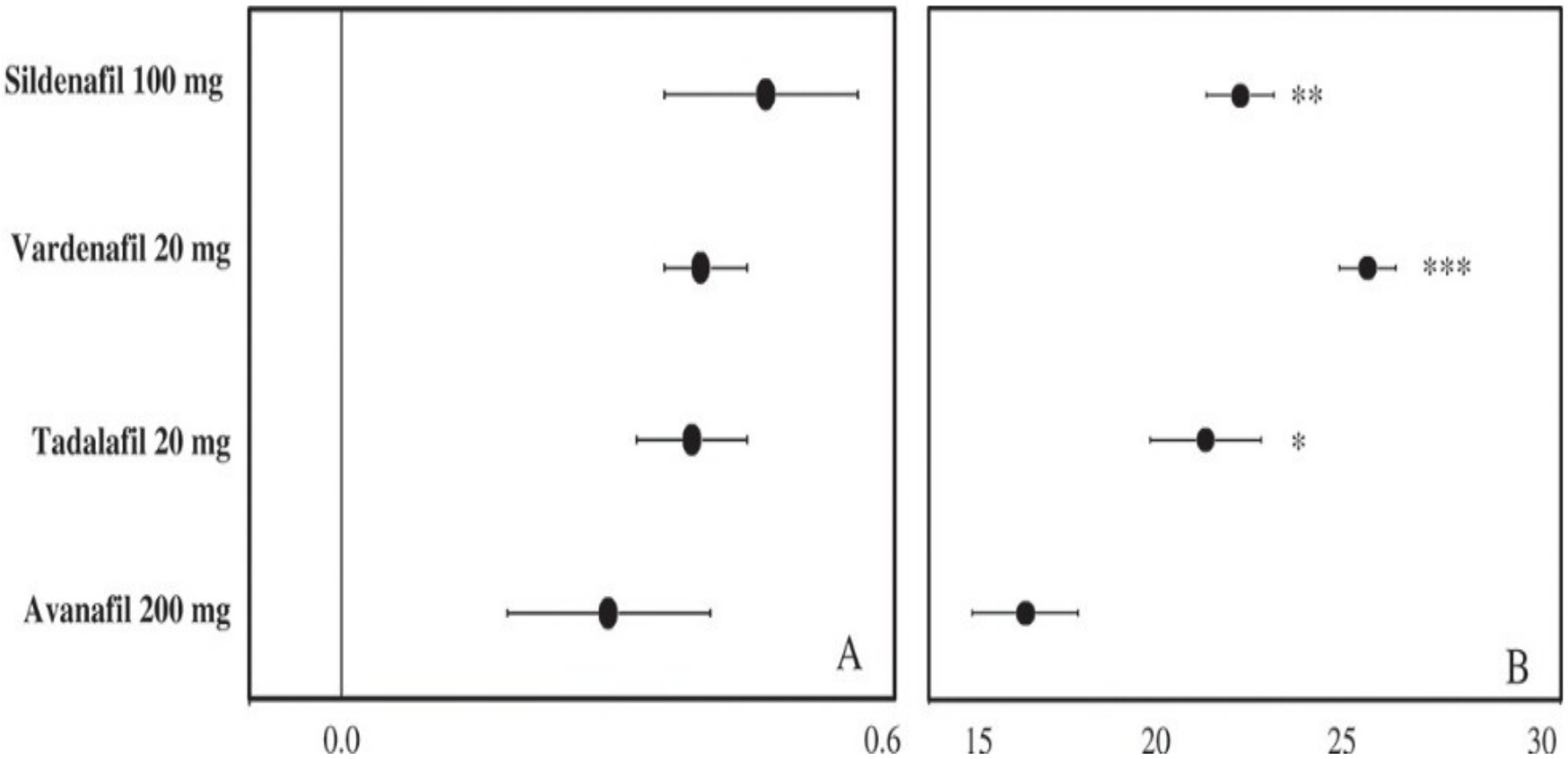
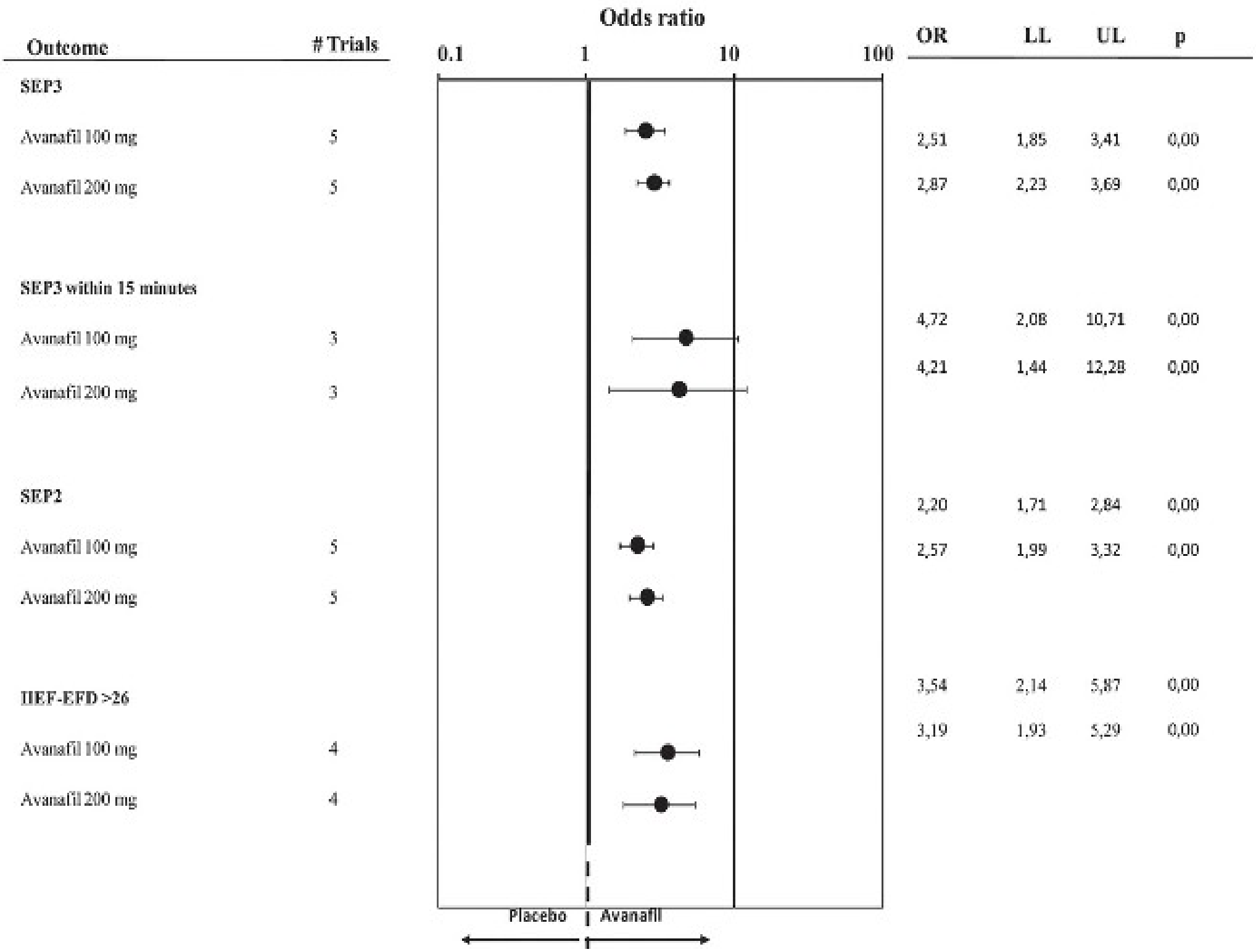
The safety and efficacy of Avanafil, a new 2nd generation PDE5i: comprehensive review and meta-analysis

Giovanni Corona, Giulia Rastrelli, Andrea Burri, Emmanuele A. Jannini & Mario Maggi

Figure 1 of 3

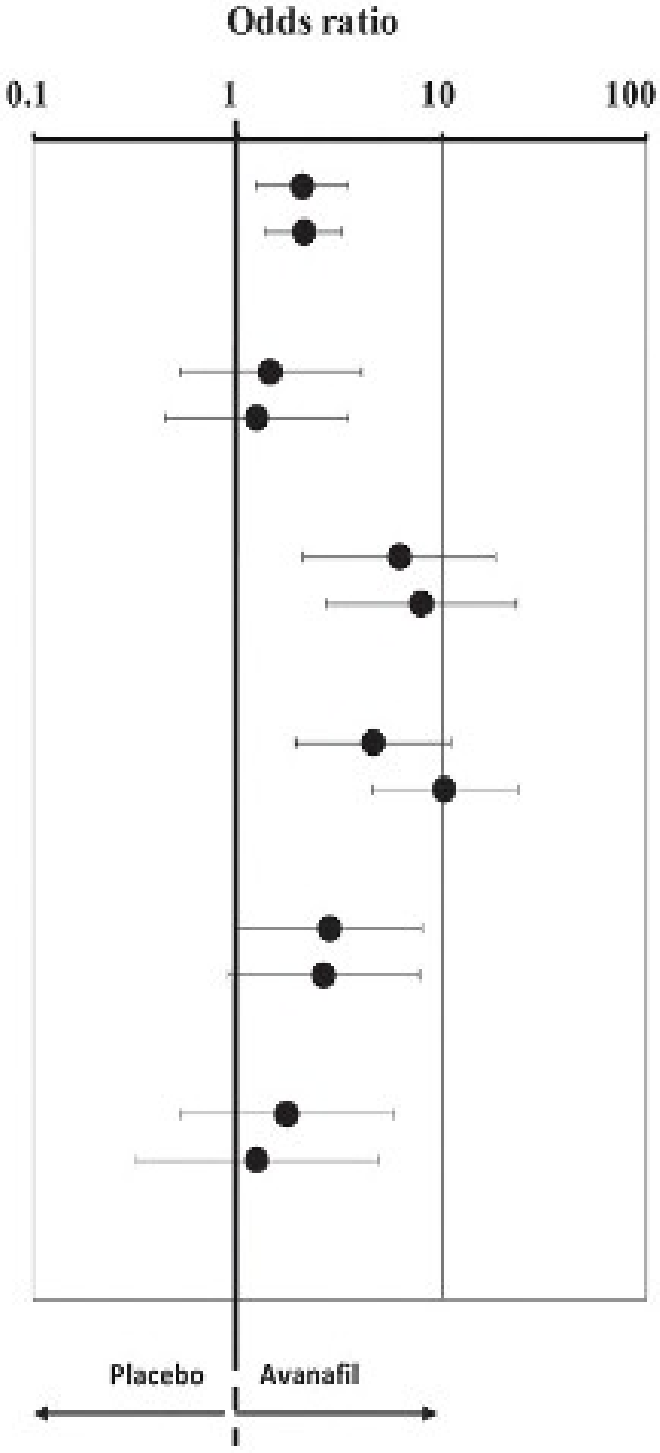
Figure 1. Panel A, shows the relative efficacy against placebo of different phosphodiesterase 5 Inhibitors (PDE5is) at the maximal recommended dose, as derived from the meta-analysis by Chen et al.[5] An overall outcome was considered by averaging four outcomes, including Sexual Encounter Profile (SEP) 2, SEP3, Global Assessment Question (GAQ)1 and normalization of International Index of Erectile Function- erectile function domain (IIEF-EFD) score (> 26). p = NS. Panel B, shows the frequency of adverse events reported when different PDE5is were used at the maximal recommended dose, as reported in the meta-analysis by Chen et al.[5] *p < 0.02, **p = 0.001, ***p < 0.0001, all vs. Avanafil.





Outcome	# Trials	OR	LL	UL	p
SEP3					
Avanafil 100 mg	5	2,51	1,85	3,41	0,00
Avanafil 200 mg	5	2,87	2,23	3,69	0,00
SEP3 within 15 minutes					
Avanafil 100 mg	3	4,72	2,08	10,71	0,00
Avanafil 200 mg	3	4,21	1,44	12,28	0,00
SEP2					
Avanafil 100 mg	5	2,20	1,71	2,84	0,00
Avanafil 200 mg	5	2,57	1,99	3,32	0,00
IIEF-EFD >26					
Avanafil 100 mg	4	3,54	2,14	5,87	0,00
Avanafil 200 mg	4	3,19	1,93	5,29	0,00

Outcome	# Trials	OR	LL	UL	p
Any AE					
Avanafil 100 mg	5	2,07	1,23	3,48	0,01
Avanafil 200 mg	5	2,10	1,35	3,26	0,00
AE leading drug discontinuation					
Avanafil 100 mg	3	1,45	0,52	4,03	0,48
Avanafil 200 mg	4	1,24	0,44	3,50	0,68
Flushing					
Avanafil 100 mg	5	6,17	2,08	18,32	0,00
Avanafil 200 mg	5	7,91	2,71	23,04	0,00
Headache					
Avanafil 100 mg	5	4,57	1,91	10,94	0,00
Avanafil 200 mg	5	10,21	4,50	23,17	0,00
Nasal congestion					
Avanafil 100 mg	5	2,81	0,99	8,01	0,05
Avanafil 200 mg	5	2,63	0,89	7,73	0,08
Back pain					
Avanafil 100 mg	3	1,74	0,53	5,72	0,36
Avanafil 200 mg	3	1,24	0,32	4,83	0,76



Avanafil - A further step to tailoring patient needs and expectations

Luca Boeri, Paolo Capogrosso, Eugenio Ventimiglia, Alessandro Serino, Giovanni La Croce, Andrea Russo, Rocco Damiano, Francesco Montorsi & Andrea Salonia

Table 1. Summary of pharmacokinetics of avanafil, sildenafil, vardenafil and tadalafil *

Parameter	Avanafil	Sildenafil	Vardenafil	Tadalafil
T_{max} (min)	30-45	60	60	120
Onset of action (min)	15-30	60	25-60	30
Effect of food on t_{max} (hr)	Delayed by 1.25 h[#]	Delayed by 1h	Delayed by 1h[#]	None
$T_{1/2}$ (hr)	6-17	3-5	4-5	17.5
Duration of action (hr)	>6[**]	4-5[§]	4-8[##]	36
Metabolism	Hepatic (CYP3A4)	Hepatic (CYP3A4)	Hepatic (CYP3A4)	Hepatic (CYP3A4)
Mode of excretion	Feces (63%), urine (21%)	Feces (80%), urine (13%)	Feces (91%-95%), urine (2%-6%)	Feces (61%), urine (36%)

ACCEPTED MANUSCRIPT

Effect on exposure/clearance of	Avanafil	Sildenafil	Vardenafil	Tadalafil
Age	None	Reduced clearance	Reduced clearance	Reduced clearance
Mild hepatic impairment	None	Increased exposure	Increased exposure	None
Moderate hepatic impairment	Reduced exposure	Increased exposure	Increased exposure	None
Severe hepatic impairment	Not studied	Not studied	Not studied	Limited data
Mild renal impairment	None	None	None	Increased exposure
Moderate renal impairment	None	None	None	Increased exposure
Severe renal impairment	No data	Increased exposure	Increased exposure	Increased exposure
Drug interactions				
CYP3A4 inhibitors	Increased exposure	Increased exposure	Increased exposure	Increased exposure
Nitrates	Potentiate hypotensive effect – (Contraindicated)	Potentiate hypotensive effect – (Contraindicated)	Potentiate hypotensive effect – (Contraindicated)	Potentiate hypotensive effect – (Contraindicated)
Alpha blockers	May lead to symptomatic hypotension (haemodynamic stability and start PDE5I at lowest dose)	May lead to symptomatic hypotension (haemodynamic stability and start PDE5I at 25mg dose)	May lead to symptomatic hypotension (haemodynamic stability and start PDE5I at lowest dose)	May lead to symptomatic hypotension (haemodynamic stability and start PDE5I at lowest dose). Association with doxazosin is contraindicated.
Acetyl salicylic acid	None	None	None	None
Antidiabetic drugs	None	None	None	None

ACCEPTED MANUSCRIPT

Adverse event	Avanafil 200 mg	Sildenafil 100 mg	Vardenafil 20 mg	Tadalafil 20 mg
Headache	9.3%	12.8%	16%	14.5%
Flushing	3.7%	10.4%	12%	4.1%
Dyspepsia	Uncommon	4.6%	4%	12.3%
Nasal congestion	1.9%	1.1%	10%	4.3%
Dizziness	0.6%	1.2%	2%	2.3%
Abnormal vision	None	1.9%	<2%	-------
Back pain	<2%	-------	--------	6.5%
Myalgia	<2%	-------	--------	5.7%

ACCEPTED MANUSCRIPT

Farmaci per la disfunzione erettile:

- alprostadil
- avanafil
- sildenafil
- tadalafil
- vardenafil

Nota 75

La prescrizione di **inibitori della PDE5** (avanafil, sildenafil, tadalafil, vardenafil) a carico del SSN è limitata ai pazienti con disfunzione erettile neurogena da lesione incompleta del midollo spinale o del plesso pelvico, di origine traumatica, infiammatorio/degenerativa o iatrogena (in seguito a chirurgia o radioterapia della regione pelvica), secondo un piano terapeutico redatto da specialisti (andrologo, endocrinologo, neurologo, urologo) afferenti al SSN.

La prescrizione di **alprostadil per iniezione intracavernosa** a carico del SSN è limitata ai pazienti con disfunzione erettile da lesioni complete del midollo spinale, e ai pazienti con disfunzione erettile neurogena da lesione incompleta del midollo spinale o del plesso pelvico qualora vi sia mancata risposta, intolleranza o contro-indicazione agli inibitori della PDE5, secondo un piano terapeutico redatto da specialisti (andrologo, endocrinologo, neurologo, urologo) afferenti al SSN.

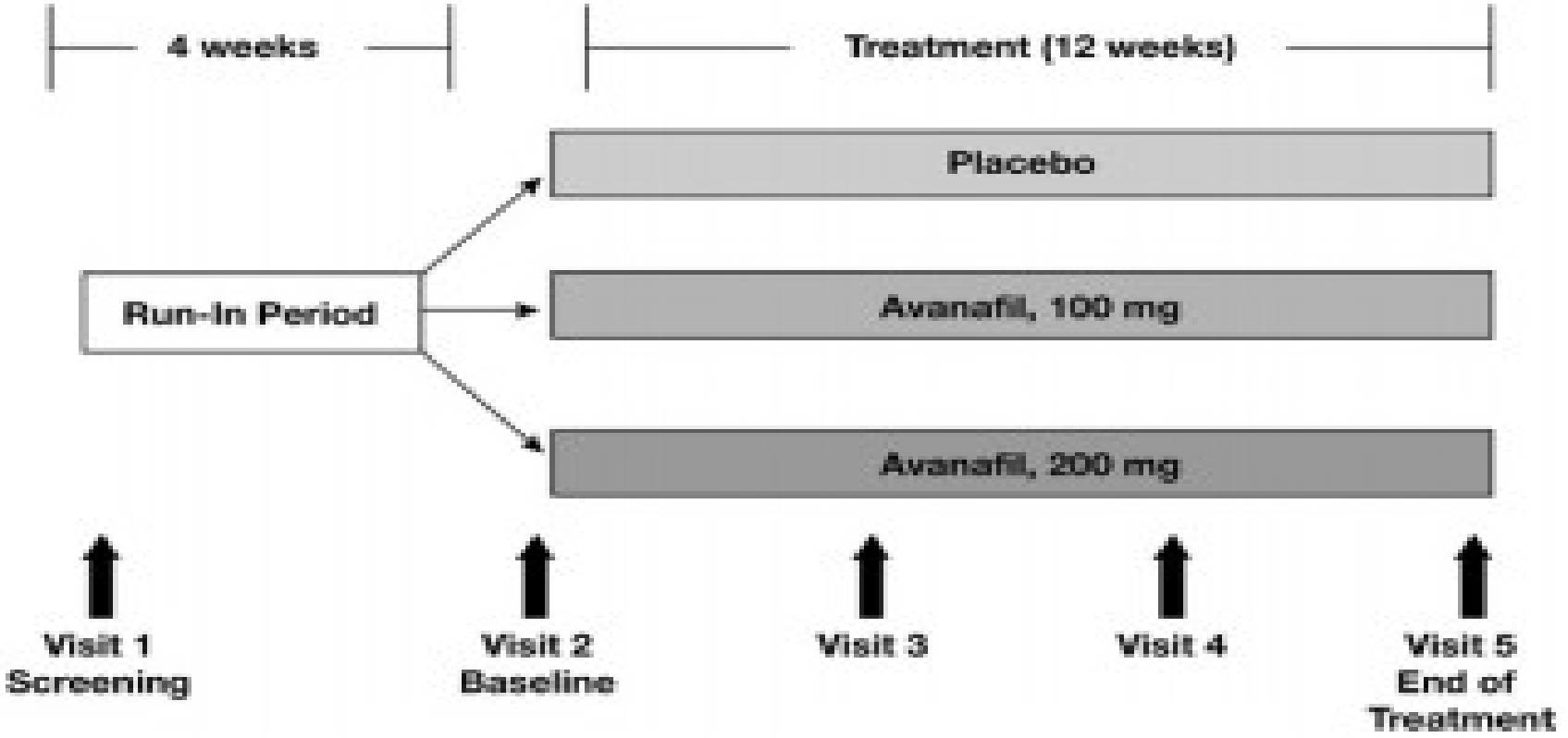
A Phase 3, Placebo Controlled Study of the Safety and Efficacy of Avanafil for the Treatment of Erectile Dysfunction After Nerve Sparing Radical Prostatectomy

THE JOURNAL of UROLOGY®
Official Journal of the American Urological Association

John P. Mulhall,*,† Arthur L. Burnett,‡ Run Wang,§ Kevin T. McVary,‖ Judd W. Moul,¶ Charles H. Bowden,** Karen DiDonato,** Winnie Shih** and Wesley W. Day**

A total of 298 patients were randomized

100 or 200 mg avanafil or placebo (taken 30 minutes before sexual activity) for 12 weeks.



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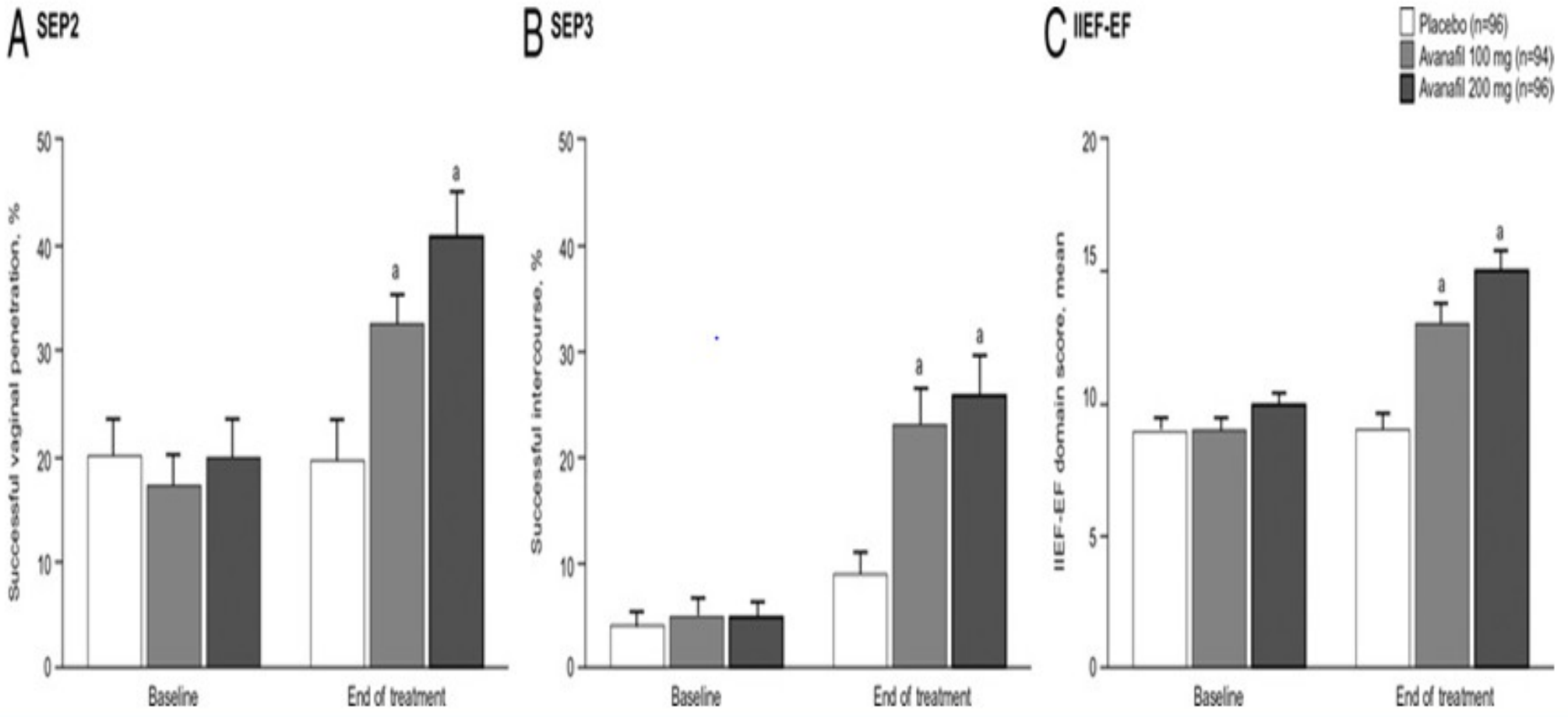

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Table 3. *Responder analysis: change from baseline scores (ITT population)*

	Placebo	Avanafil 100 mg	Avanafil 200 mg
No. pts	96	94	96
SEP3:			
No. (%)*	14 (14.6)	26 (27.7)	36 (37.5)
p Value	Not applicable	0.5	<0.01§
SEP2:			
No. (%)†	7 (7.3)	29 (30.9)	37 (38.5)
p Value	Not applicable	0.01§	<0.01§
IIEF-EF:			
No. (%)‡	13 (13.7)	33 (35.1)	48 (50.0)
p Value	Not applicable	<0.01§	<0.01§

* Responders with a change from baseline of 23% or greater.

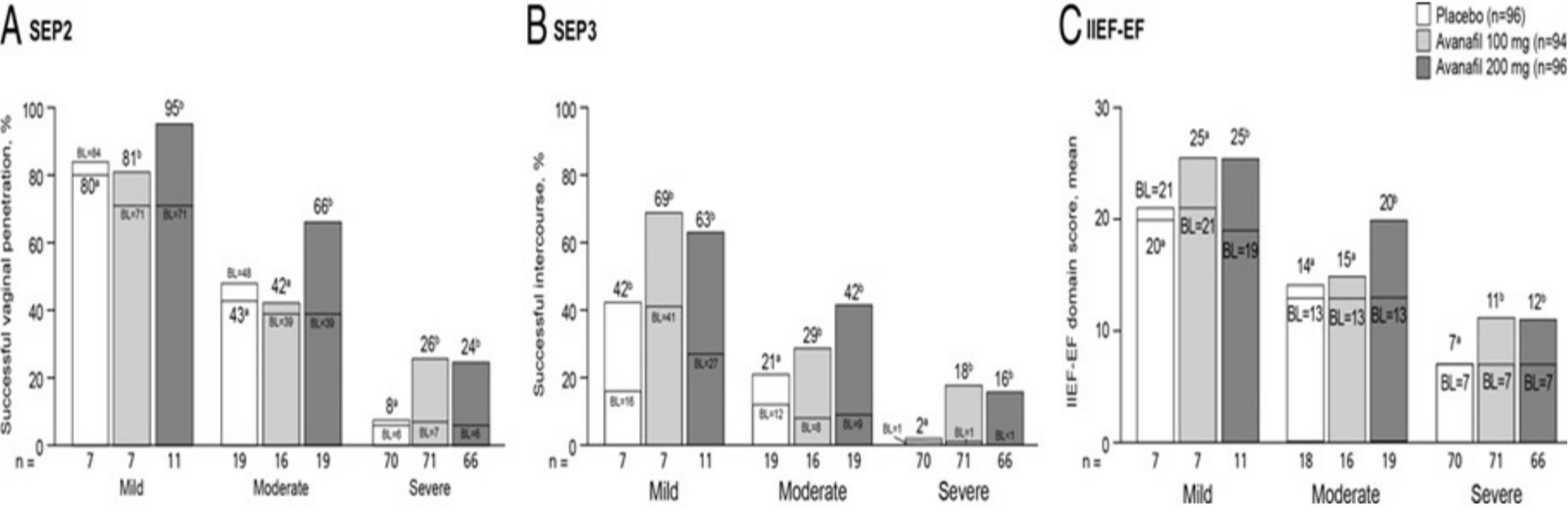

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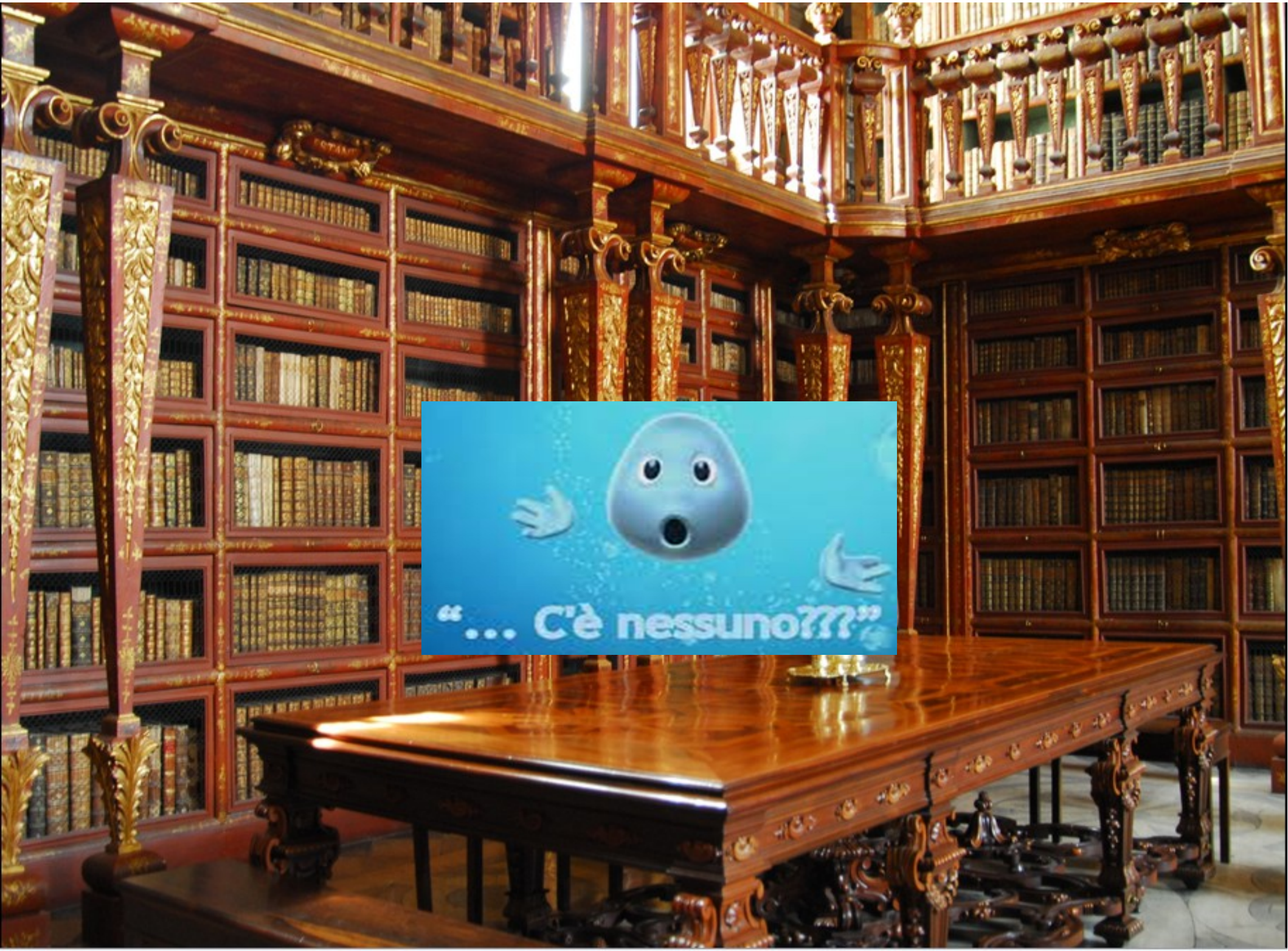
Table 2. *All TEAEs reported in 1% or more of patients (safety population)*

	No. Placebo (%)	No. Avanafil 100 mg (%)	No. Avanafil 200 mg (%)	No. Totals (%)
Headache	1 (1.0)	8 (8.1)	12 (12.1)	21 (7.0)
Flushing	0 (0.0)	5 (5.1)	10 (10.1)	15 (5.0)
Nasopharyngitis	0 (0.0)	3 (3.0)	5 (5.1)	8 (2.7)
Back pain	1 (1.0)	3 (3.0)	2 (2.0)	6 (2.0)
Nasal congestion	1 (1.0)	3 (3.0)	1 (1.0)	5 (1.7)
Upper respiratory tract infection	0 (0.0)	2 (2.0)	3 (3.0)	5 (1.7)
Abnormal electrocardiogram	0 (0.0)	1 (1.0)	3 (3.0)	4 (1.3)
Bronchitis	4 (4.0)	0 (0.0)	0 (0.0)	4 (1.3)
Dizziness	0 (0.0)	1 (1.0)	2 (2.0)	3 (1.0)
Blood cholesterol increased	1 (1.0)	2 (2.0)	0 (0.0)	3 (1.0)
Nausea	1 (1.0)	1 (1.0)	1 (1.0)	3 (1.0)

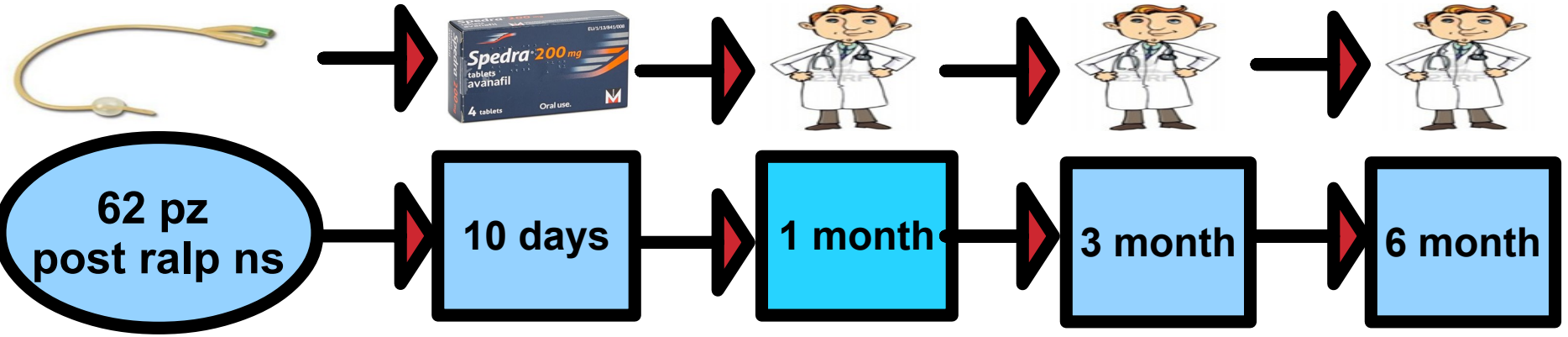
TEAEs were defined as AEs occurring after the first dose of study drug or after the first dispense date, if missing, and before the last visit.

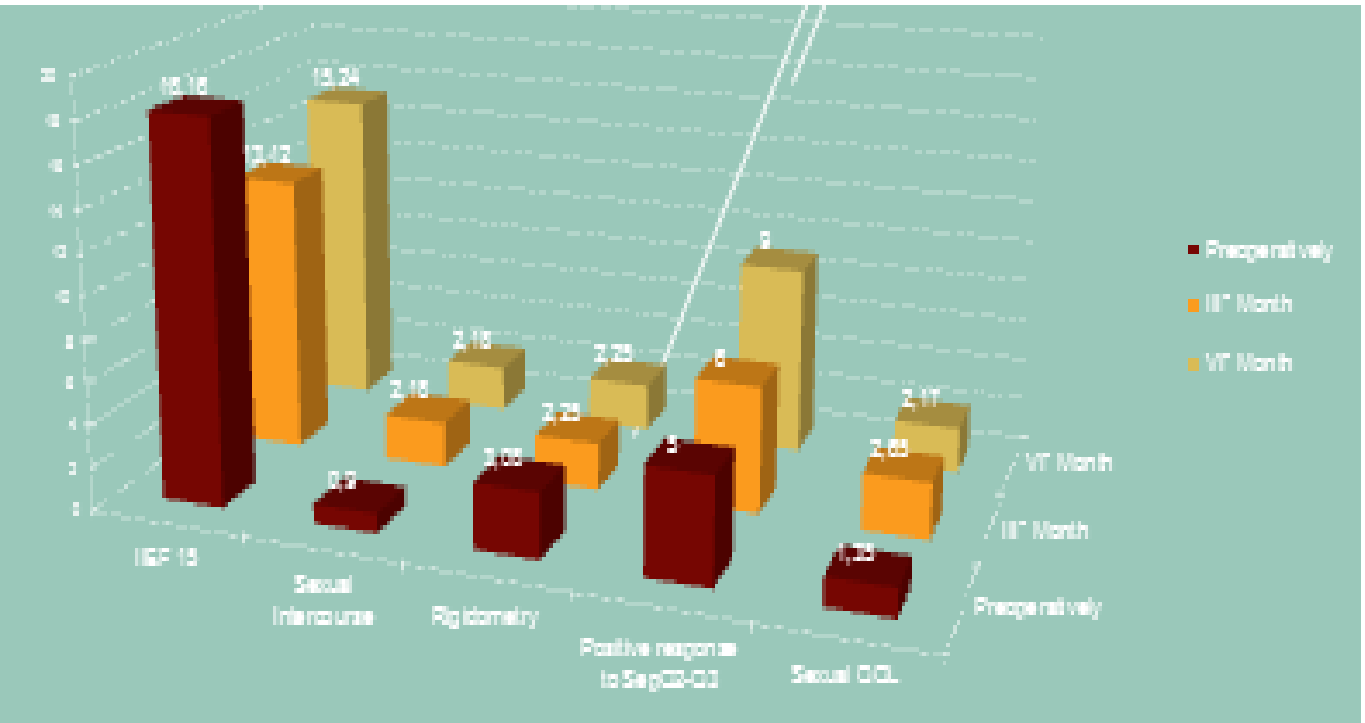

“... C’è nessuno???”

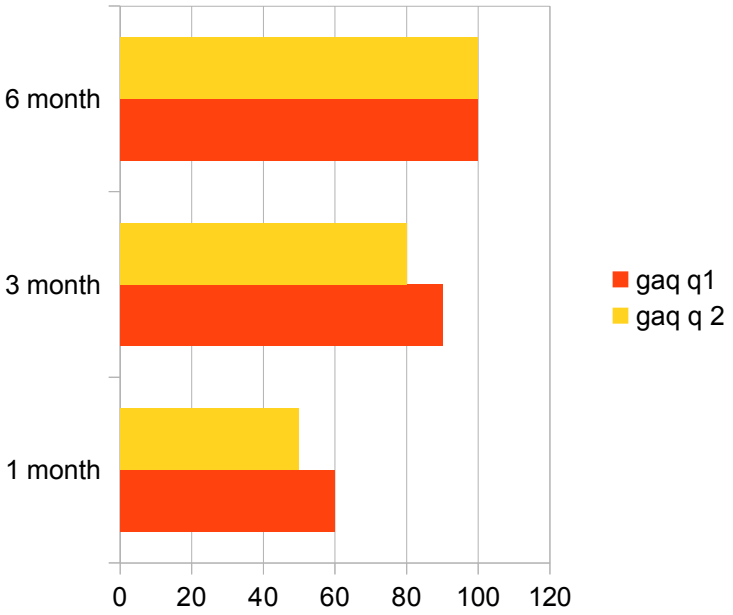
AVANAFIL 200 mg three times a week in sexual rehabilitation after monolateral nerve-sparing prostatectomy: Efficacy and Tolerability after six months of chronic therapy

Pier Andrea Della Camera, Gianmartin Cito, Simone Morselli, Nicola Laruccia, Andrea Cocci, Riccardo Campi, Mauro Gacci, Marco Carini, Sergio Serni, Alessandro Natali

Dipartimento di Urologia, Università degli Studi Di Firenze, A.O.U. Careggi, Firenze.







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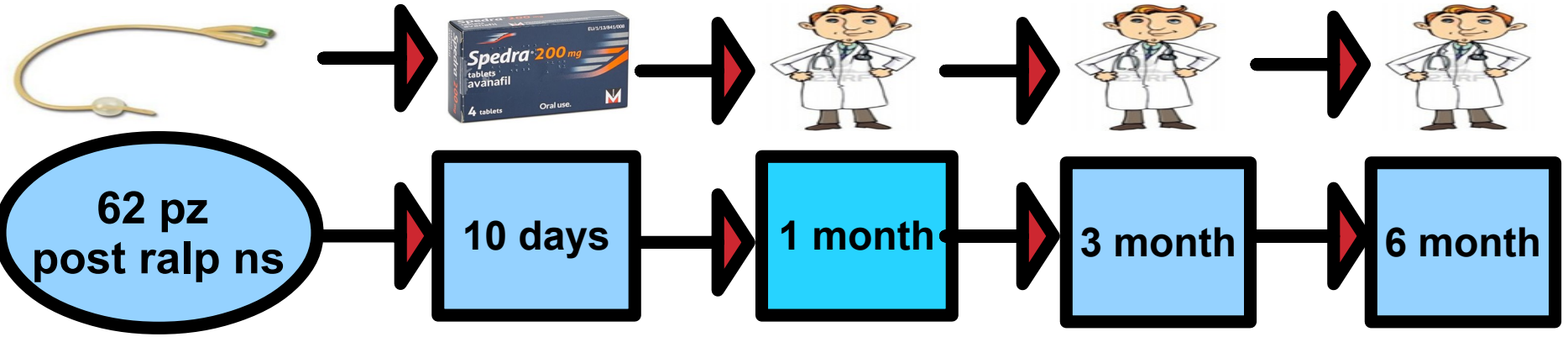

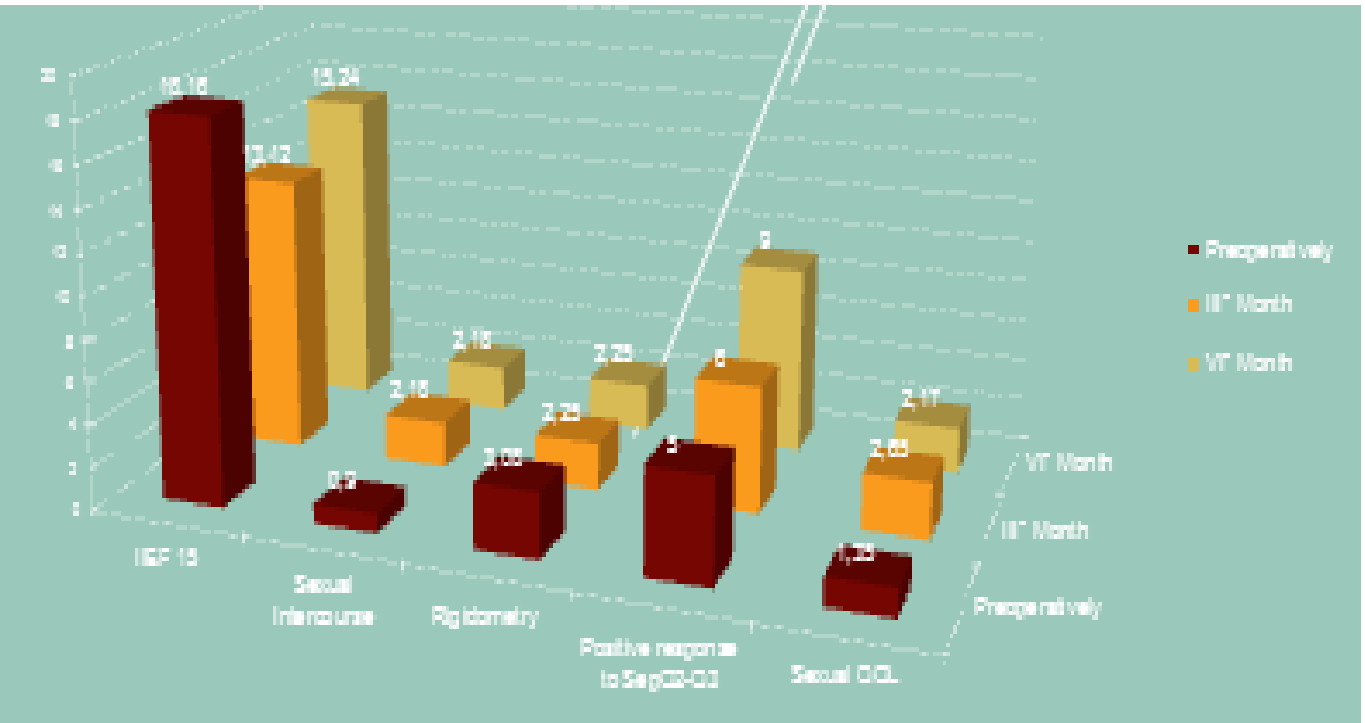

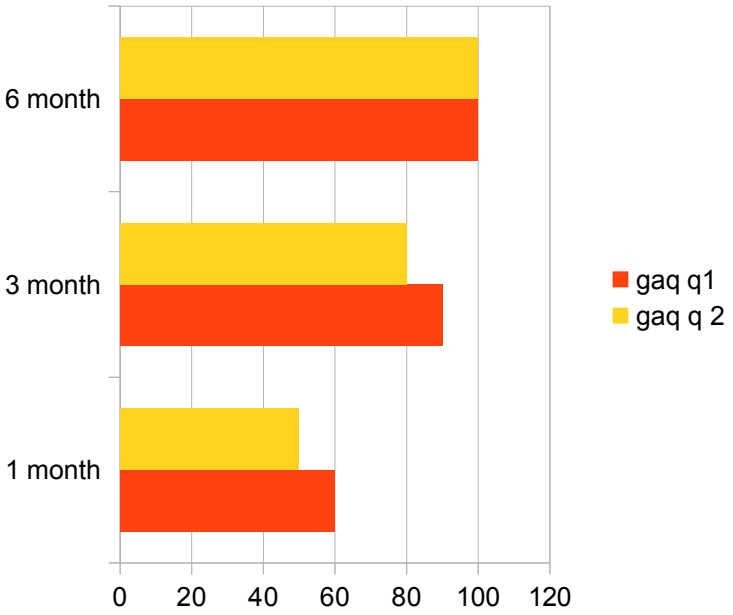

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Quali sono le novità ?

- Introduzione dei tests gaq
- Introduzione del rigidometro
- Utilizzo dell iief 15
- Valutazione del numero dei rapporti settimanali
- Valutazione della Sexual quality of Life
- Lungo Follow Up
- Valutazione dell'attivita' farmacologica bed time

Limiti dello studio:

- Piccolo campione in esame

Nuovi pde-5 orosolubili

Doxapharma
UN DELTA IN PIU'

Sildenafil	**Vardenafil**
Viagra orodispersibile 50 mg (pfizer)	**Levita orodispersibile** 10 mg (bayer)
Siler (sofar) **Rabestrom(ibsa)** -25mg - 50 mg - 75 mg -100 mg	

per il trattamento della DE[1]

- C'è un alto **tasso di abbandono**, fino all'80%[6]
- Un terzo degli uomini che assume PDE5i ne interrompe l'assunzione dopo la prima prescrizione e metà entro 6 mesi[7]
- Spesso il farmaco non corrisponde alle aspettative del paziente[8]

Anche se gli uomini che assumono un inibitore della PDE5 per la DE riportano un certo grado di soddisfazione con il trattamento, circa la metà dei pazienti mostra un certo grado di insoddisfazione[4]

La terapia ideale: una scelta impossibile o una mirata impostazione sartoriale?

SILDENAFIL 2017:
film orodispersibile

Bibliografia 1. Hatzimouratidis K et al. Guidelines on Male Sexual Dysfunction: Erectile Dysfunction and Premature Ejaculation. European Association of Urology 2015; 2. Nicolosi A et al. Urology 2003; 61(1): 201-6. 3. Capogrosso P et al. J Sex Med 2013; 10: 1833-41. 4. Jannini EA et al. J Sex Med 2014; 11(1): 40-50. 5. Kubin M et al. Int J Impot Res 2003; 15 (1): 63-71. 6. Corona G et al. Andrology 2016; 4: 1062-69. 7. Mirone V et al. J Sex Med 2013; 10: 1861-66. 8. Jann BP et al. Int J Impot Res 2006; 18(2): 145-9.

SOFAR

RESEARCH ARTICLE Swapnil L.Patil et al, IJRRPAS, 2(3):482-496, ISSN 2249-1236

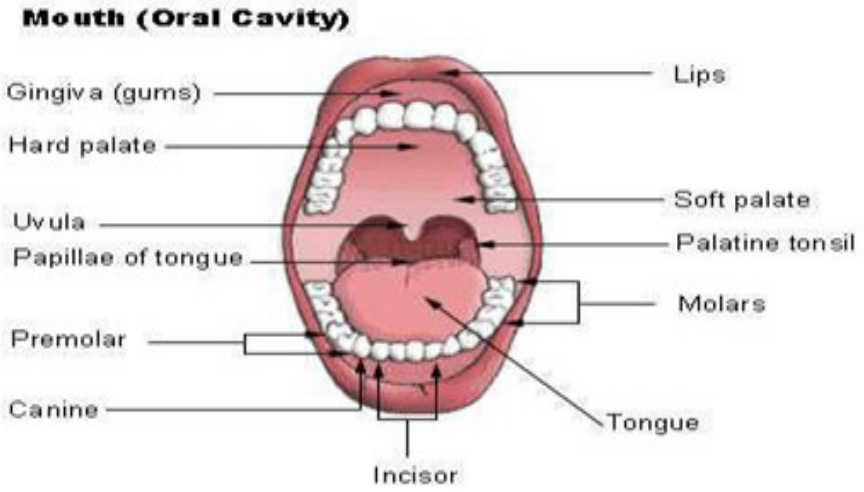
International Journal of Research and Reviews in Pharmacy and Applied science

www.ijrrpas.com

Swapnil L. Patil*, Paresh R. Mahaparale, Madhavi A. Shivnikar, Shradha S. Tiwari, Ketan V. Pawar, Prashant N. Sane

FAST DISSOLVING ORAL FILMS: AN INNOVATIVE DRUG DELIVERY SYSTEM

ABSTRACT



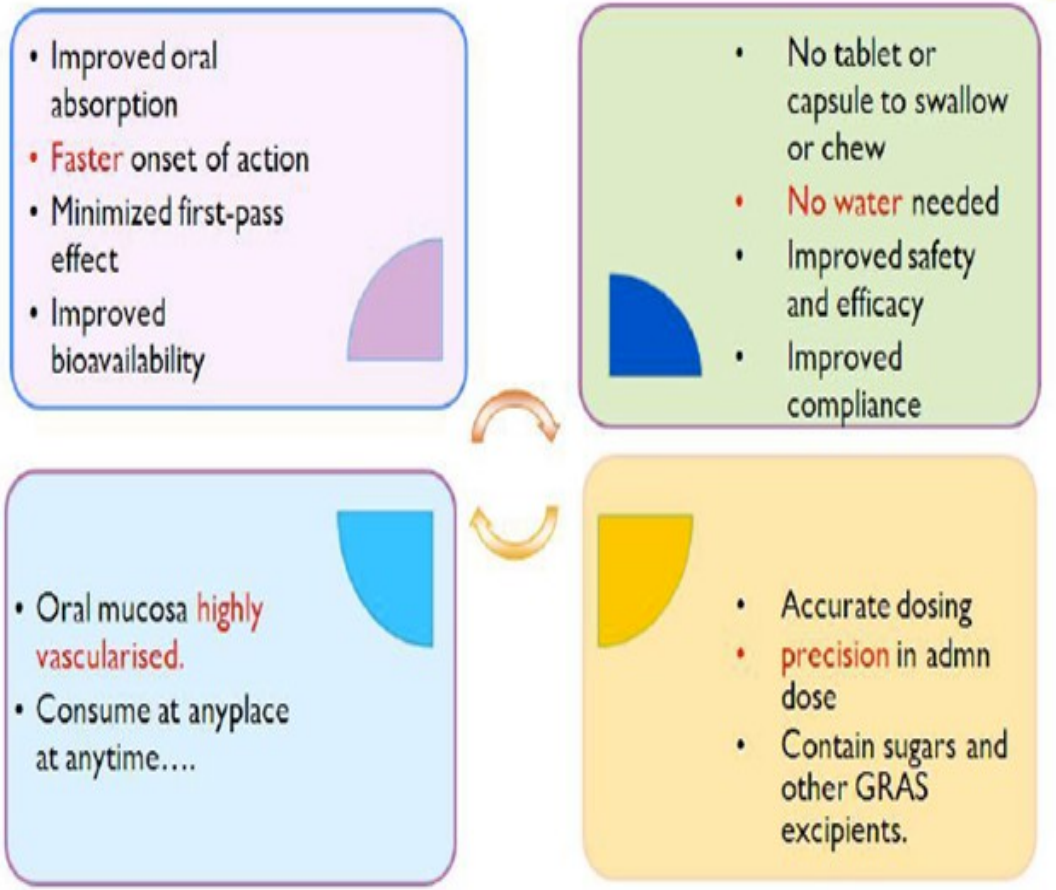


Fig 1: Advantages Of FDF

IN LETTERATURA E' BEN DOCUMENTATA ANCHE LA POSSIBILITA' DI SOMMINISTRARE FORMULAZIONI ORODISPERSIBILI PER VIA SUBLINGUALE E TRANSMUCOSA

SCOPO PRINCIPALE DI TALI VIE DI SOMMINSITRAZIONE E' RAPPRESENTATO DALLA RAPIDITA' DI AZIONE DEL FARMACO.

ALCUNI RICERCATORI SOSTENGONO CHE CON TALE SOMMINSITRAZIONE SI OTTERREBBERO RISULTATI OTTIMALI CON MINORI DOSAGGI DEL FARMACO

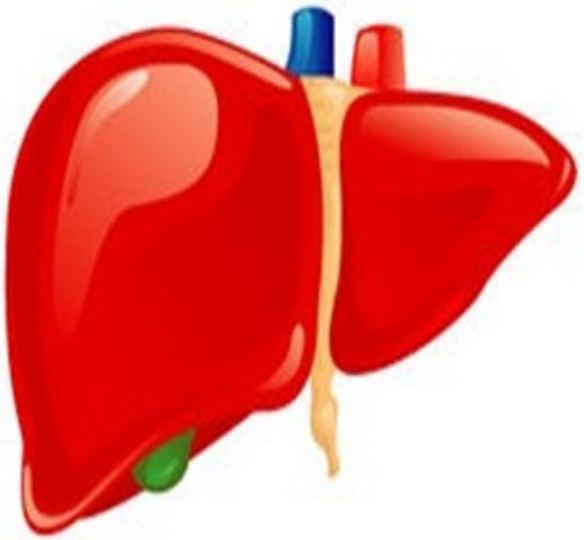
Amancha KP, 2015; Deveci S, 2004; Goswami T, 2008; Huang X, 2009

I farmaci assunti attraverso tale via evitano il metabolismo di "primo passaggio" epatico raggiungendo rapidamente picchi plasmatici elevati

Il farmaco non viene alterato !

E’ bene inoltre ricordare che dopo la normale somministrazione orale, solo il 41% del farmaco (Sildenafil) e’ stato individuato in circolo (biodisponibilità), segno che la maggior parte viene inattivata a livello epatico !

(RCP Sildenafil)



Altra ragione di tale formulazione e' la convenienza di non necessitare di acqua per la somministrazione

Short active

- Velocità
- Paziente giovane rapporto occasionale
- Potenza
- Effetti collaterali
- Durata
- Interazione cibo

Medium active

- Velocità
- Paziente giovane rapporto occasionale
- Potenza
- Effetti collaterali
- Durata
- Interazione cibo

Long active

- Velocità
- Paziente giovane rapporto occasionale
- Potenza
- Effetti collaterali
- Durata
- Interazione cibo

Riabilitazione post prostatectomia

Short active

Medium active

3 / week

Long active

2 / week

Nota 75

Riabilitazione post prostatectomia

On demand

Nota 75

Riabilitazione post prostatectomia

Giornaliero

Montorsi

Giornaliero

On demand

H. Porst

Nuova formulazione prostaglandine

-Vitaros

Pagina 26 / 29

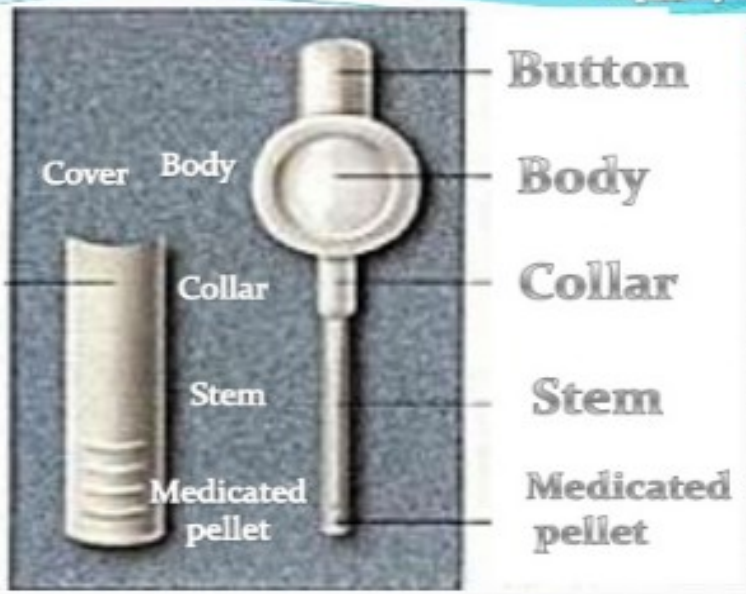
vitaros
3 mg/g
crema
alprostadil
4 ACCUDOSE

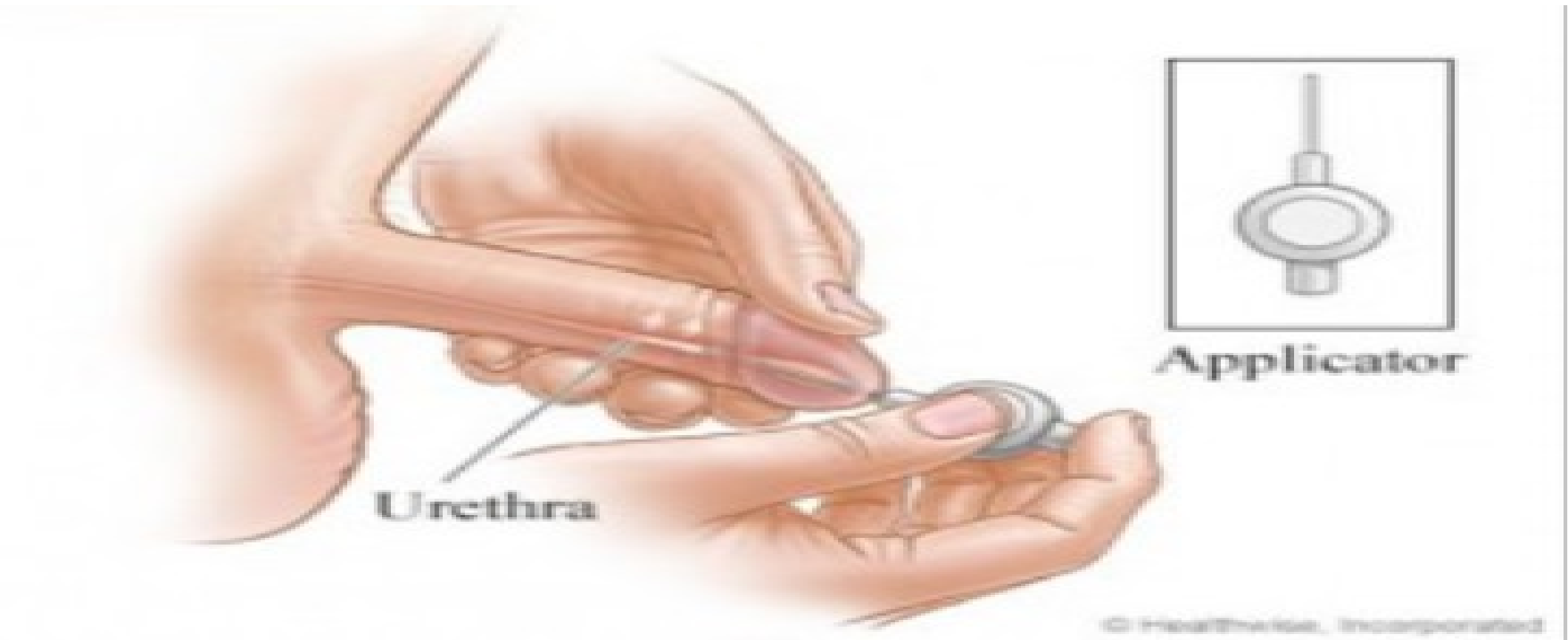
vitaros
3 mg/g
crema
alprostadil
4 ACCUDOSE

LEVOREACT OFTALMICO
0,05% Collirio, Sospensione
Levocabastina
OFTALMICO
Agitare prima dell'uso

vitaros
3 mg/g
crema
alprostadil
4 ACCUDOSE

MUSE


Button
Body
Collar
Stem
Medicated pellet
Cover
Body
Collar
Stem
Medicated pellet


Applicator
Urethra

U
ISSN 0391-5603

Urologia 2015; 82 (2): 84-92
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DRUG REVIEW

Open Access

Clinical efficacy and safety of Vitaros©/Virirec© (Alprostadil cream) for the treatment of erectile dysfunction

Ignacio Moncada[1], Béatrice Cuzin[2]

[1] Hospital La Zarzuela c/Pléyades, Madrid - Spain
[2] Department of Urology and Transplantation, Universitary E Herriot Hospital, Lyon Cedex - France

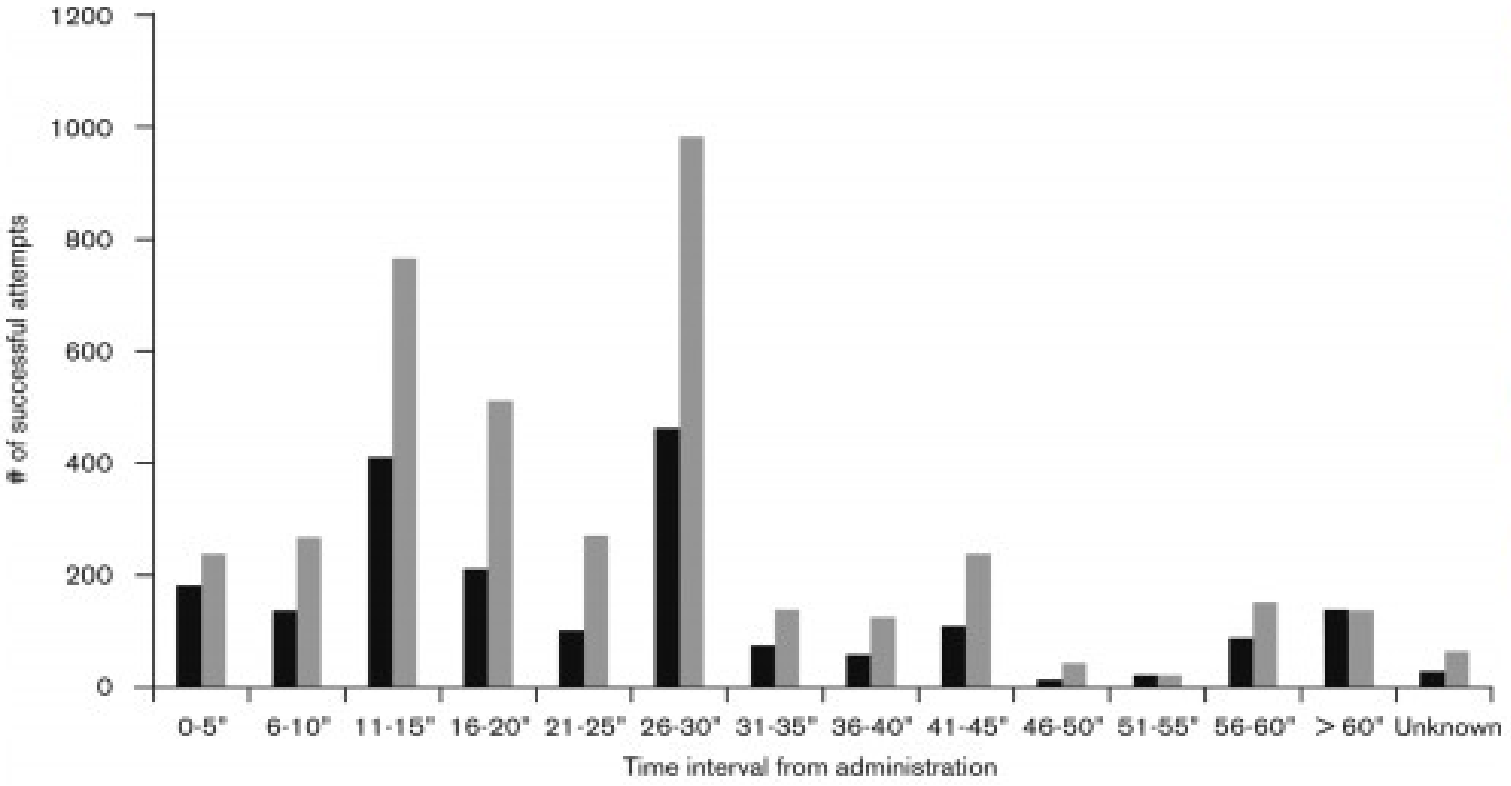

Fig. 3 - Onset of action of Vitaros©/ Virirec©. The data presented are from two multicenter, placebo-controlled, double-blind, parallel-group phase III studies conducted on a large cohort of 1732 patients (mean age 60 years) with moderate to severe ED and concomitant medical conditions. Patients were randomly assigned to receive placebo or alprostadil topical cream in doses of 100, 200, or 300 µg for 12 weeks. The number of patients is shown for each time interval considering time from administration to successful penetration attempts for the 300 µg dose.

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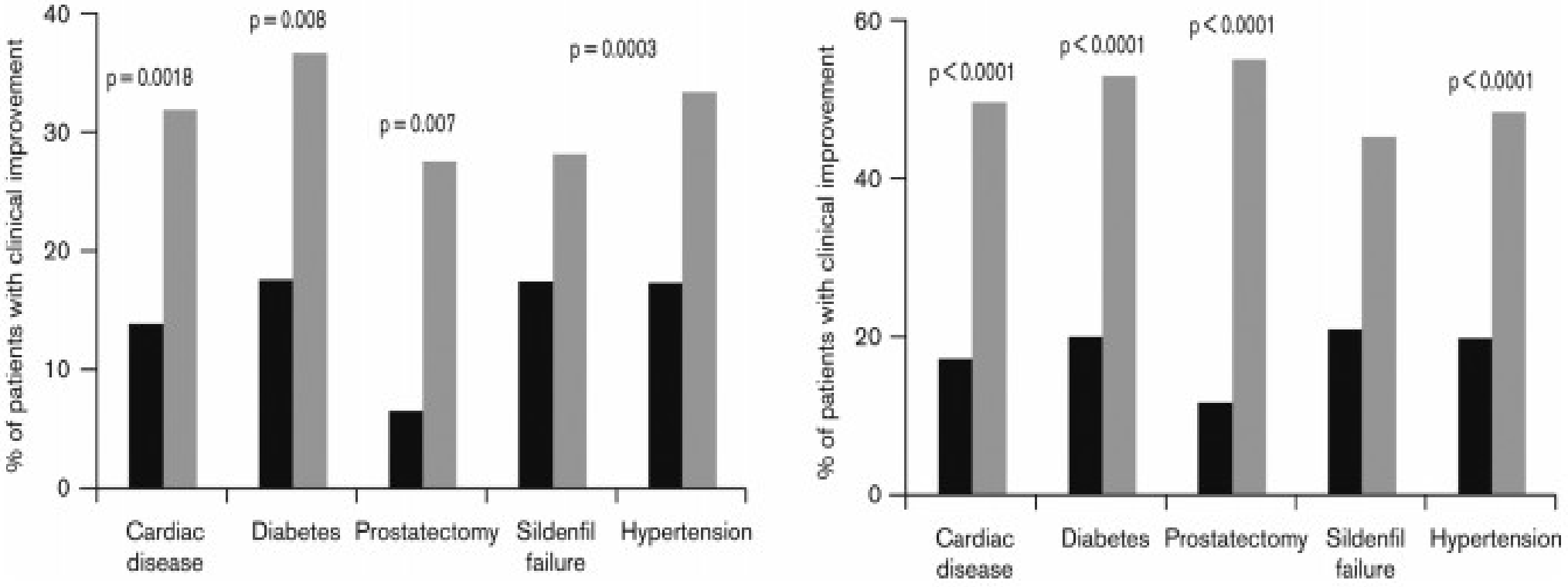

Fig. 7 - Percentage of patients with changes in IIEF-EF scores in the placebo (■) and Vitaros©/Virirec© (▫) groups with cardiac history, diabetes, prostatectomy, and hypertension (**panel A**); percentage of patients with a positive GAQ response in the control (■) and Vitaros©/Virirec© (▫) groups ($p<0.0001$ vs. placebo) (**panel B**).

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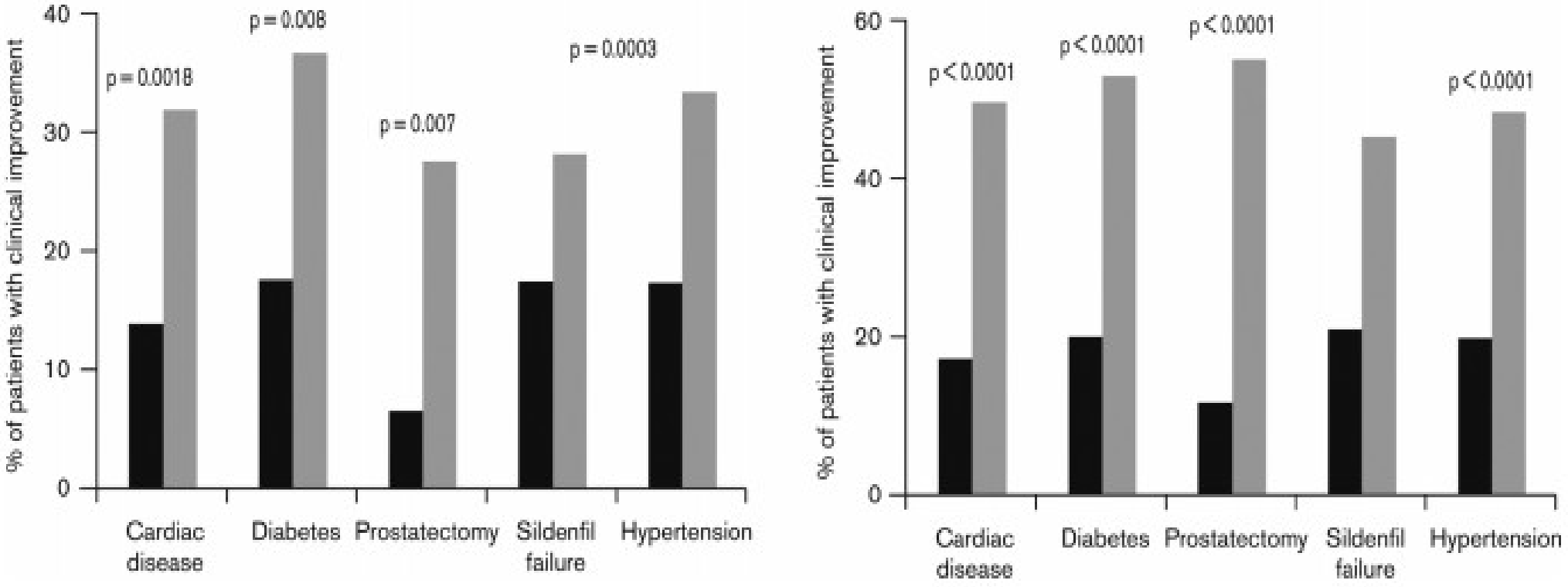

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Systemic side effects	Placebo (n = 434)	Vitaros 300 µg (n = 434)
Patient n (%)		
Total	3 (0.6)	13 (3.0)
Headache	1 (0.2)	-
Dizziness	1 (0.2)	5 (1.1)
Hyperesthesia	0 (0)	6 (1.4)
Rash	1 (0.2)	2 (0.5)

Adapted from (24).

TABLE II - Most common local (urogenital) adverse events in ed patients and partners after treatment with Vitaros©/Virirec© 300 µg

TABLE II - Most common local (urogenital) adverse events in ed patients and partners after treatment with Vitaros©/Virirec© 300 µg

Local side effects	Placebo (n = 434)	Vitaros 300 µg (n = 434)
Patient n (%)		
Total	51 (10.6)	279 (64.9)
Balanitis	3 (0.7)	20 (4.6)
Edema penile	1 (0.2)	6 (1.4)
Fullness genital	-	4 (0.9)
Genital pain	2 (0.5)	76 (17.5)
Penile burning	26 (0.6)	100 (23)
Penile erythema	9 (2.1)	49 (11.3)
Penile itching	1 (0.2)	5 (1.2)
Penile tingling	7 (1.6)	4 (0.9)
Penis disorder	2 (0.4)	15 (3.5)
Partner n (%)		
Total	13 (3)	28 (6.5)
Vaginal burning	8 (1.8)	19 (4.4.)
Vaginitis	5 (1.2)	9 (2.1)

Adapted from (24).

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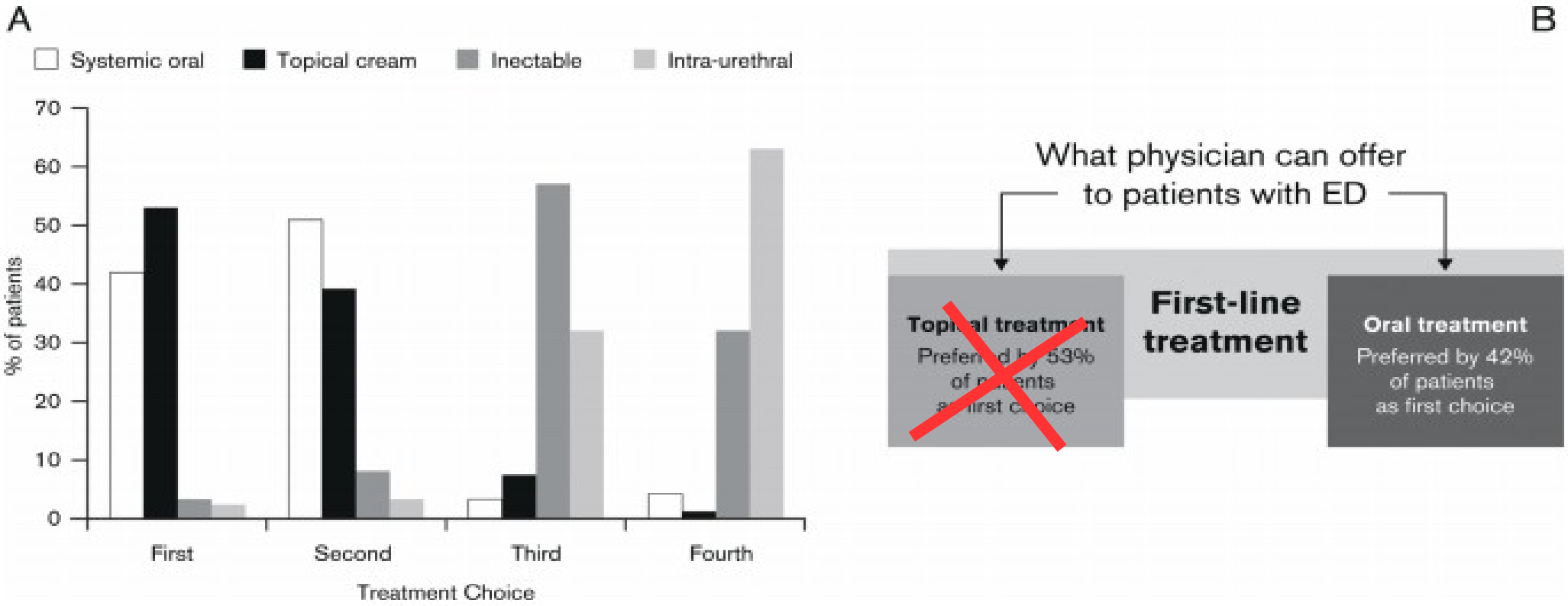


Fig. 9 - Panel A: Ranking of patient preferences (first to fourth choice) of the ideal route of administration for therapy of ED. Survey of 152 patients with ED who were asked to rank their preferred route of administration therapy for ED. **Panel B:** Schematic representation of therapeutic choices in patients with ED.

REVIEW

Current role of local treatments for erectile dysfunction in the real-life setting

Kyriakos Moisidis, Nikolaos Kalinderis, and Konstantinos Hatzimouratidis

Purpose of review
Local treatments for erectile dysfunction include intraurethral alprostadil as well as topical alprostadil cream. They are alternative treatment options to oral or intracavernosal treatments that could overcome unmet needs in patient treatment.

Recent findings
Intraurethral and topical alprostadil are two local methods of delivering an erectogenic drug to the patient. They have an established efficacy and a safety profile without important systemic adverse events. Efficacy data show that they result in significantly improved erections sufficient for sexual intercourse compared with placebo. Comparative efficacy data to other treatments are very limited. There are no specific contraindications to other drugs. They can be offered to patients who do not tolerate or do not respond to oral treatment. They can be also combined to oral treatment as a salvage therapy before proceeding to intracavernosal injections. The major advantages of them are the patient-friendly modality of delivering and the presence of minor local adverse events that are self-limited and mild in nature. Priapism or prolonged erections are very rare with local treatments.

Summary
Local treatments can have an important role as a first-line treatment for erectile dysfunction or in drug combinations mainly because of their excellent safety profile.

Keywords
alprostadil, erectile dysfunction, topical treatments

CURRENT OPINION

Current role of local treatments for erectile dysfunction in the real-life setting

Kyriakos Moisidis, Nikolaos Kalinderis, and Konstantinos Hatzimouratidis

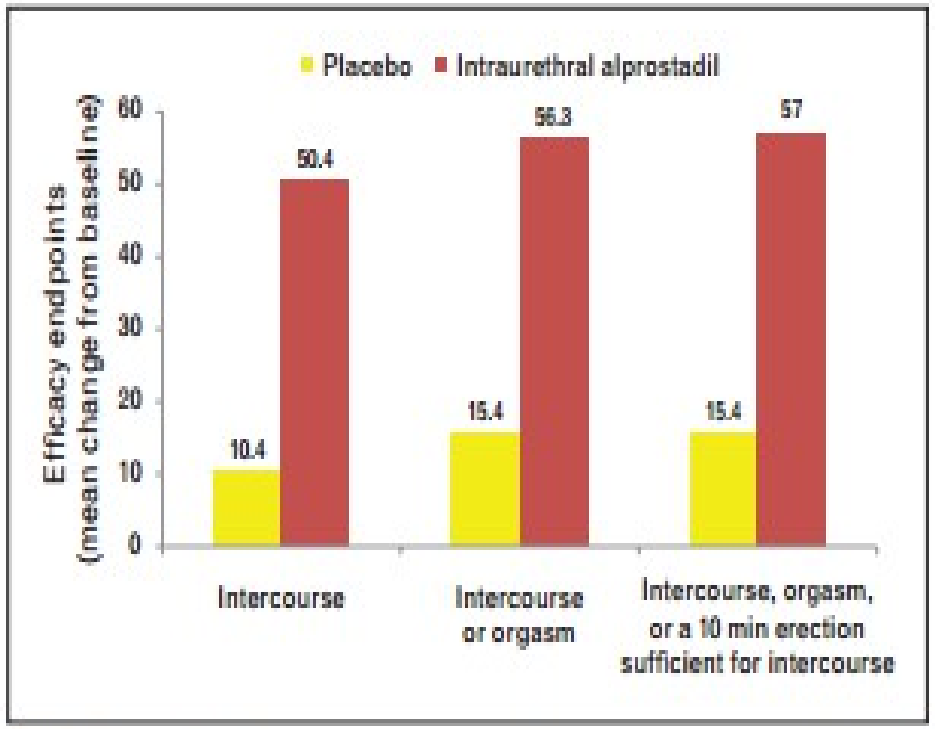


FIGURE 1. Efficacy endpoints of transurethral alprostadil versus placebo (all men, at home use. All changes were statistically significant ($P < 0.001$) [11].

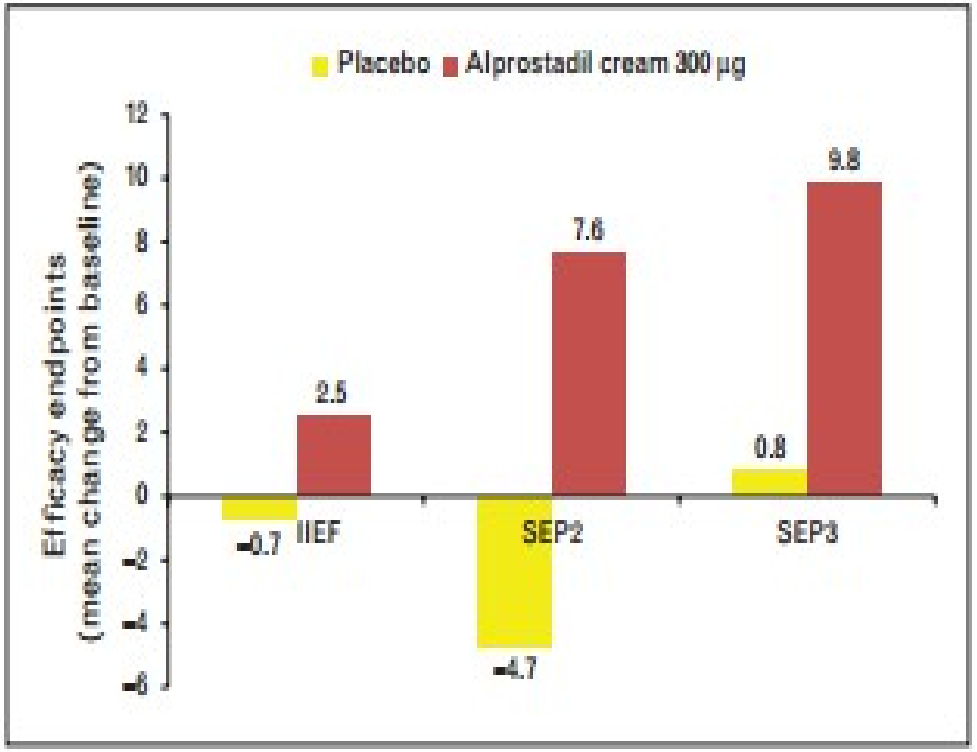


FIGURE 3. Primary efficacy end points of alprostadil cream 300 µg versus placebo. All changes were statistically significant ($P < 0.001$) [26].

Current role of local treatments for erectile dysfunction in the real-life setting

Kyriakos Moisidis, Nikolaos Kalinderis, and Konstantinos Hatzimouratidis

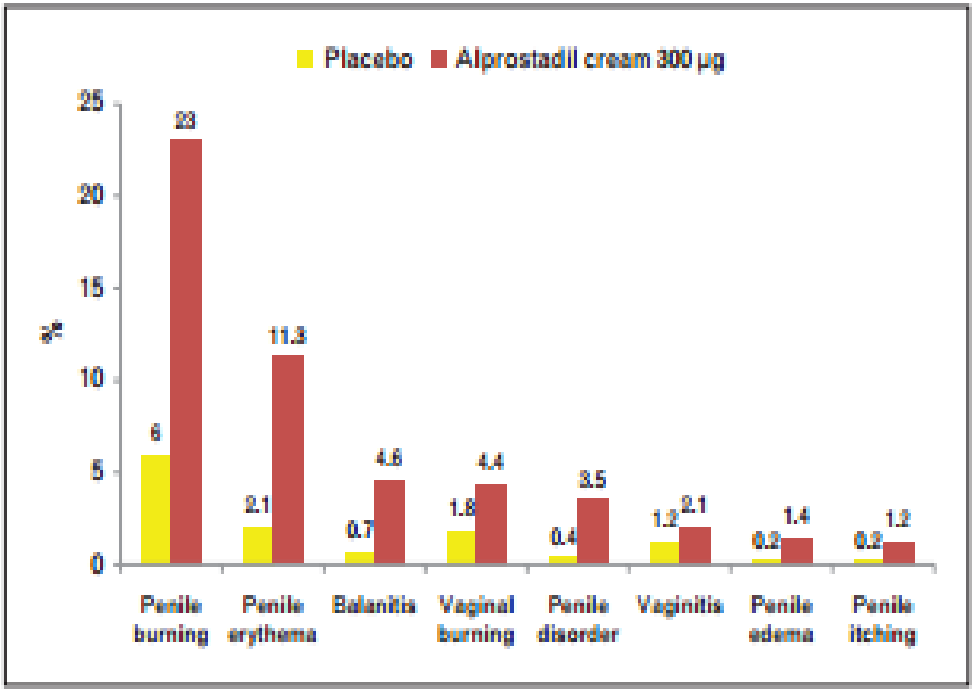


FIGURE 4. Common adverse events (>1%) of alprostadil cream 300 µg versus placebo [26]. Penile disorder includes penile throbbing, penile numbness, excessive rigidity, lack of sensation of penis tip, bent penis, and midshaft corporal plaque worsening.

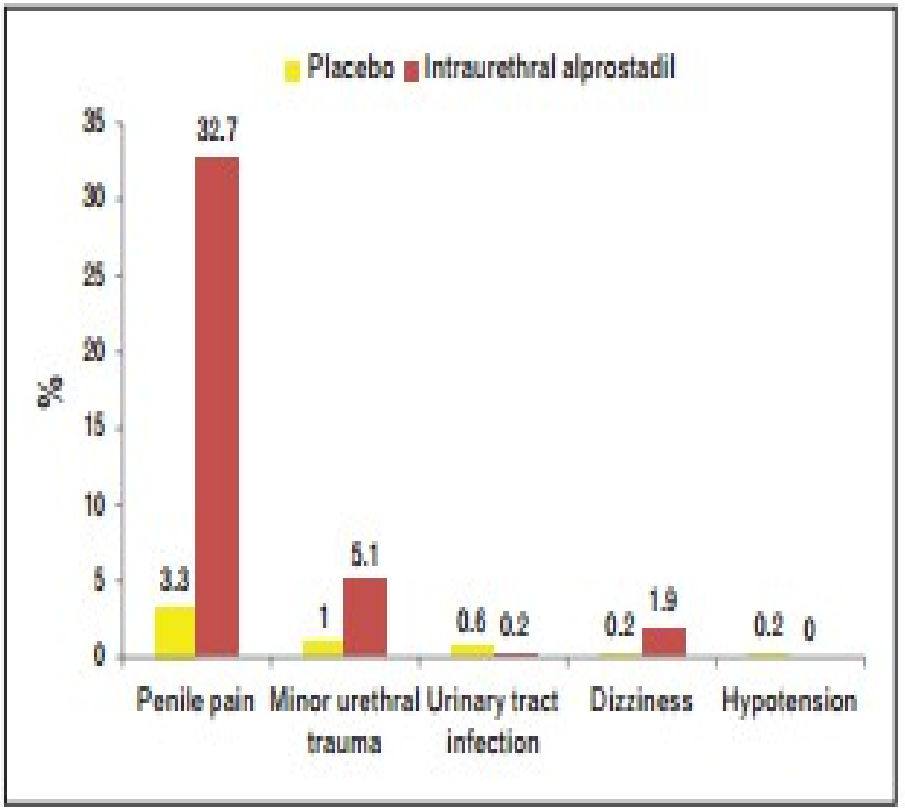


FIGURE 2. Adverse events of intraurethral alprostadil versus placebo [11].

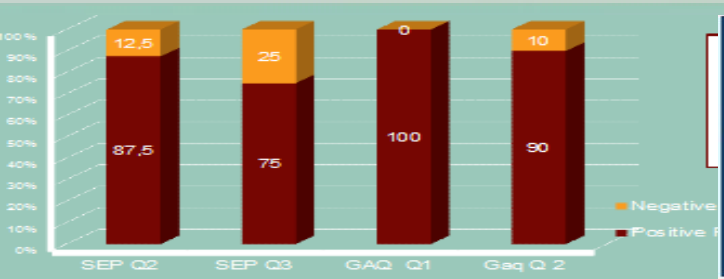
Disfunzione erettile semplice

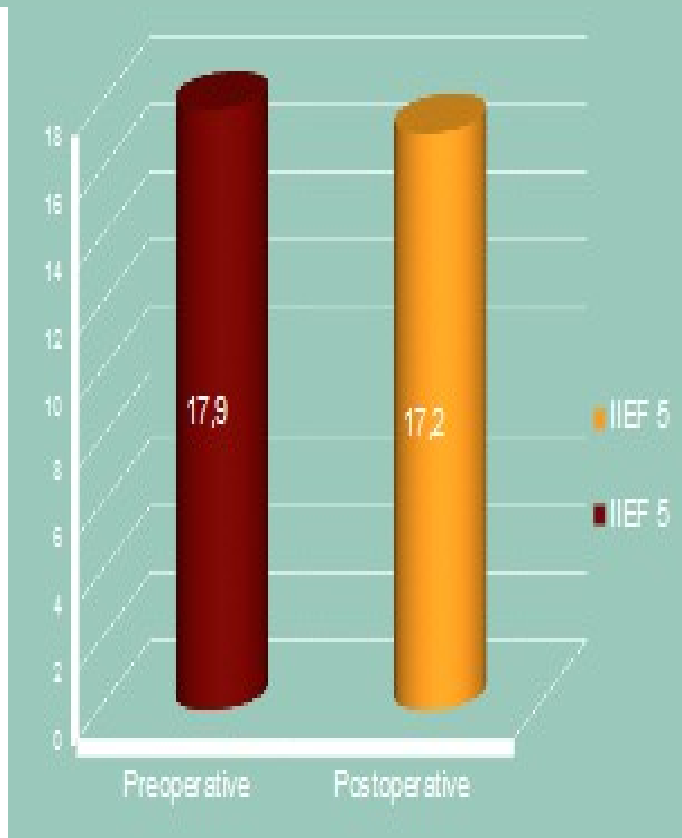
Disfunzione erettile post prostatectomia

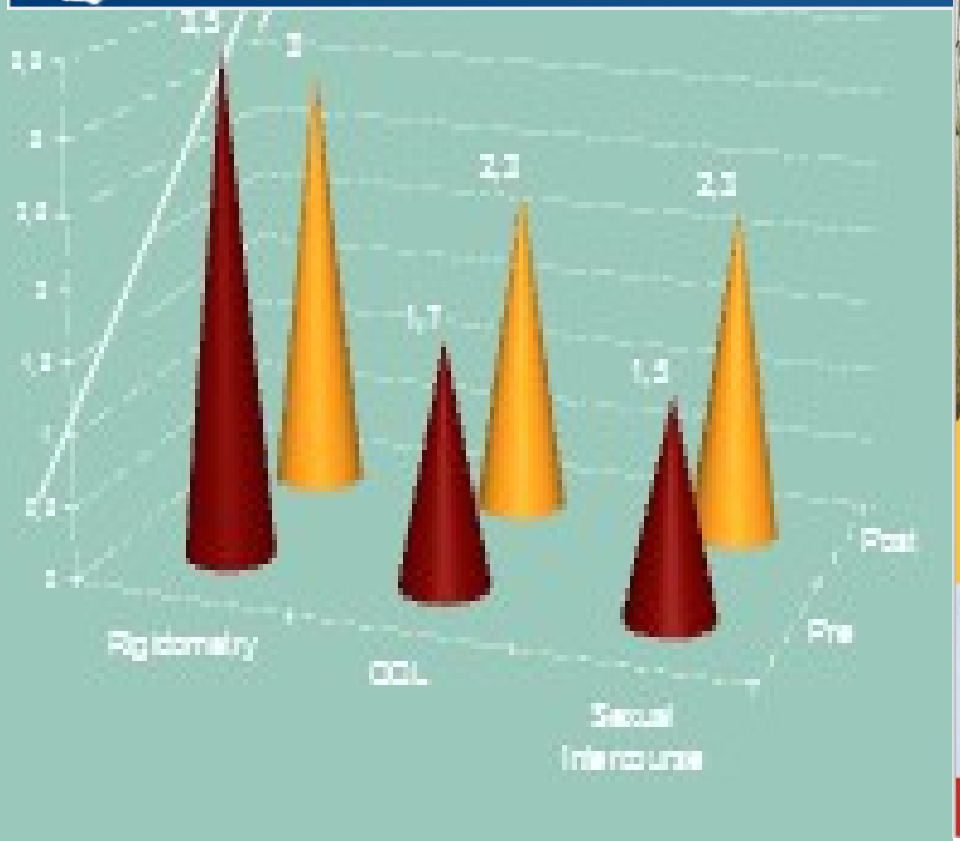
Vitaros for the treatment of post prostatectomy erectile dysfunction. An effective alternative?

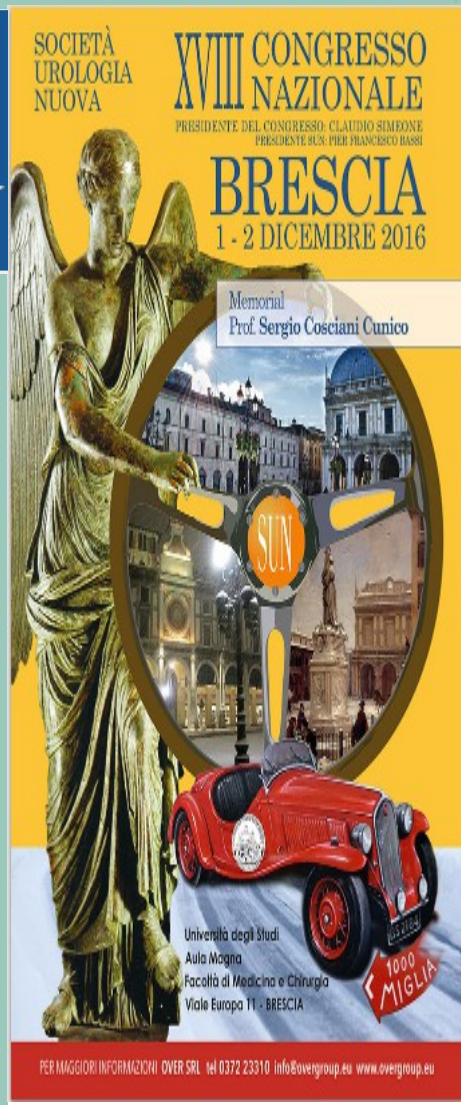
Pier Andrea Della Camera, Gianmartin Cito, Simone Morselli, Giovanni Tasso, Nicola Laruccia, Andrea Cocci, Mauro Gacci, Marco Carini, Sergio Serni, Alessandro Natali

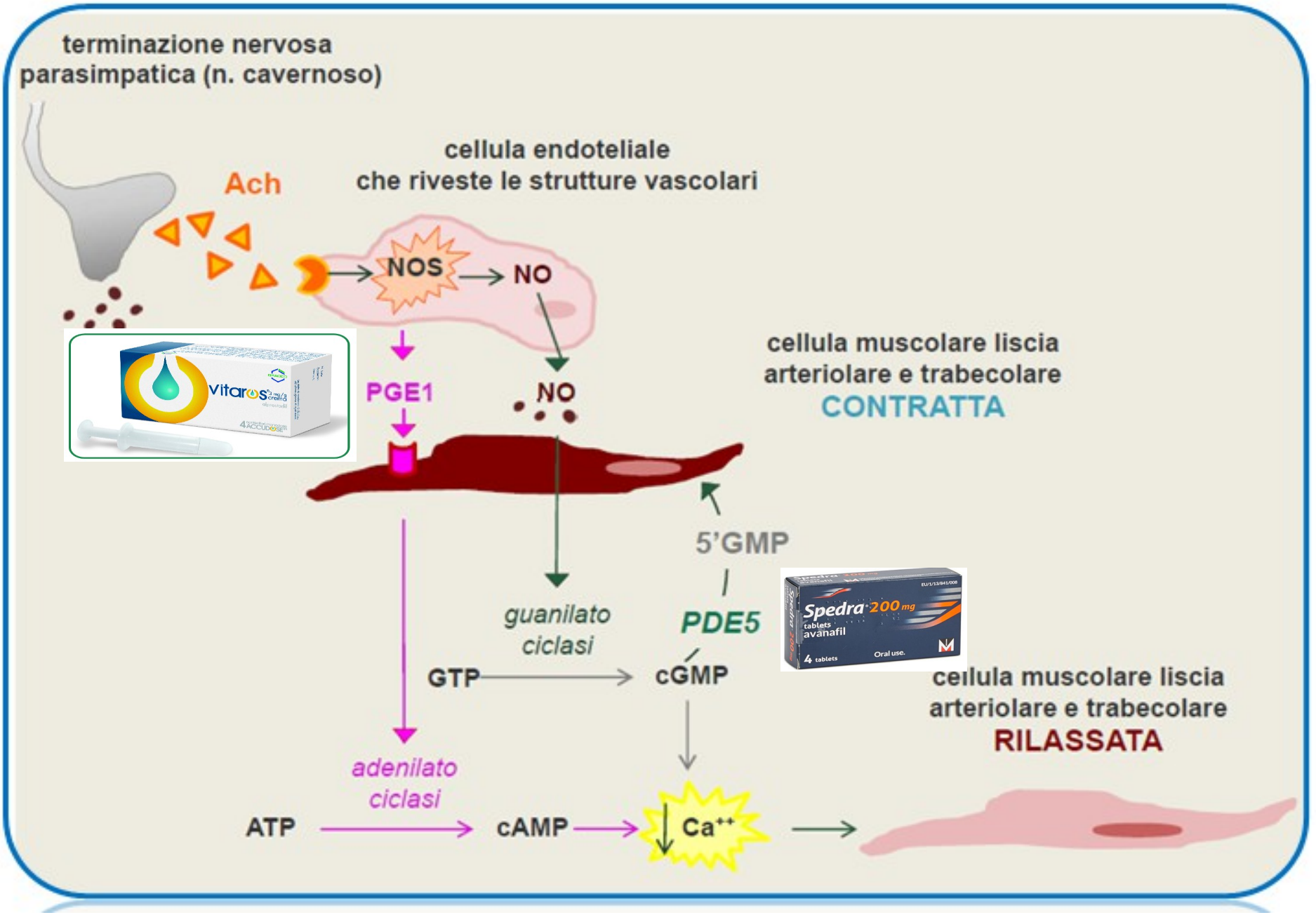
Dipartimento di Urologia, Università degli Studi Di Firenze, A.O.U. Careggi, Firenze.





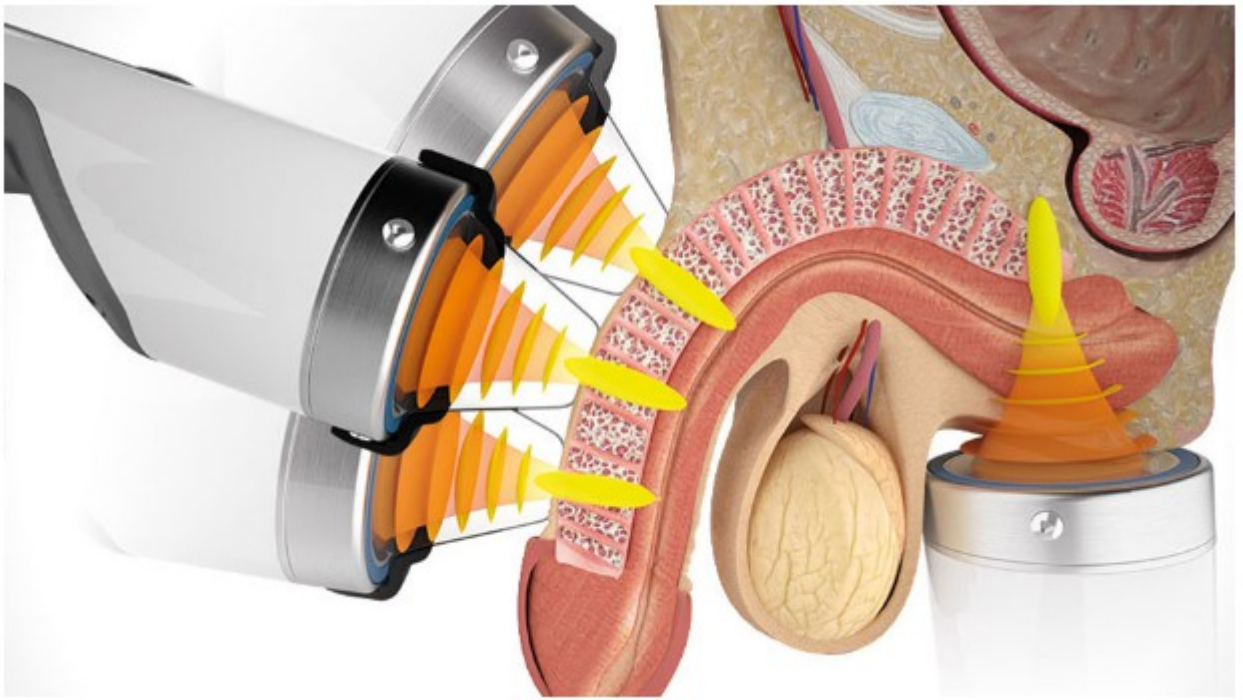






Terapia di associazione

Onde d'urto nella D.E. (Li-eswt)



6 sedute 2 a settimana con un intervallo terapeutico di 1 settimana

Potenza 0,1 max 0,25 mj/mm quadro

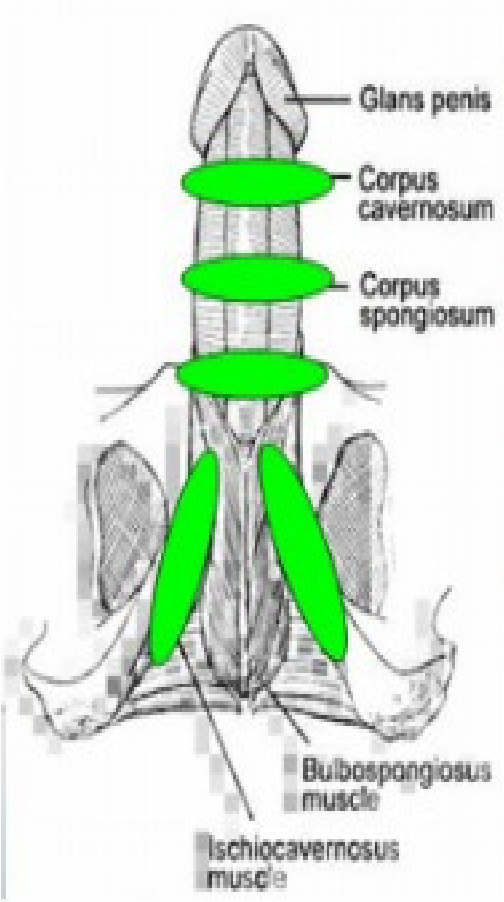
Ogni 500 colpi cambiare posizione applicatore

Posizioni consigliate: porzione distale e porziano prossimale pene bilaterlmente, crura bilateralmente

Risultati non permanenti. Da ripetere cicli ogni 2 anni

Non doloroso ottima compliance

Shaft



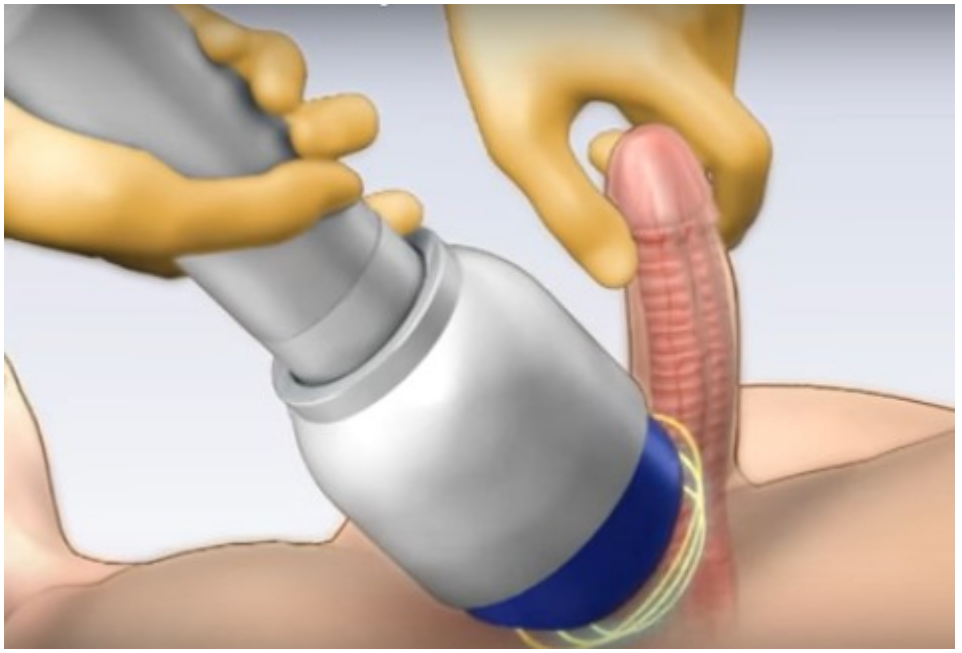
Crura

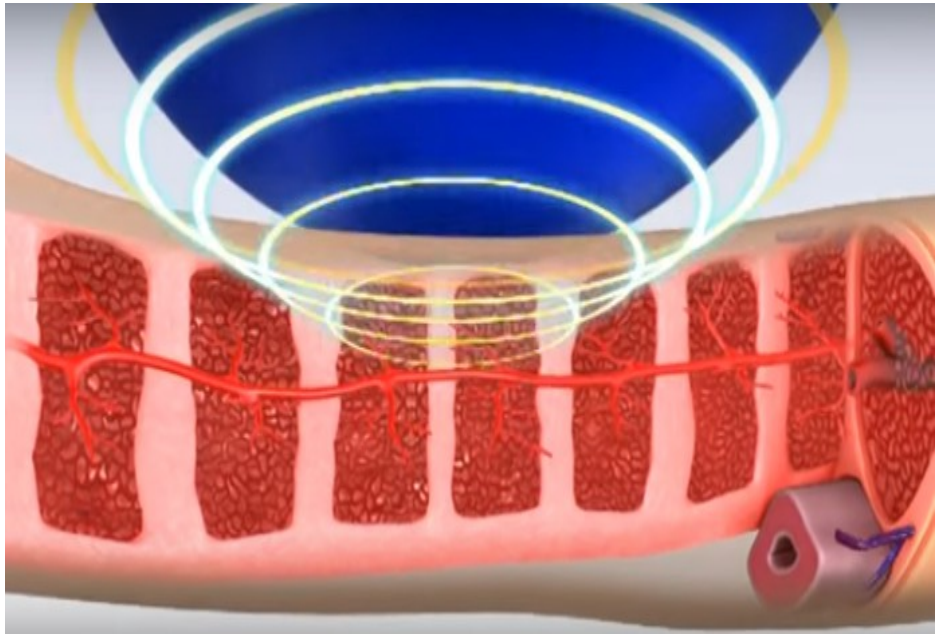
Apply 300 shocks at five locations across the shaft and crura a total of 1200 shocks per session (15 min).

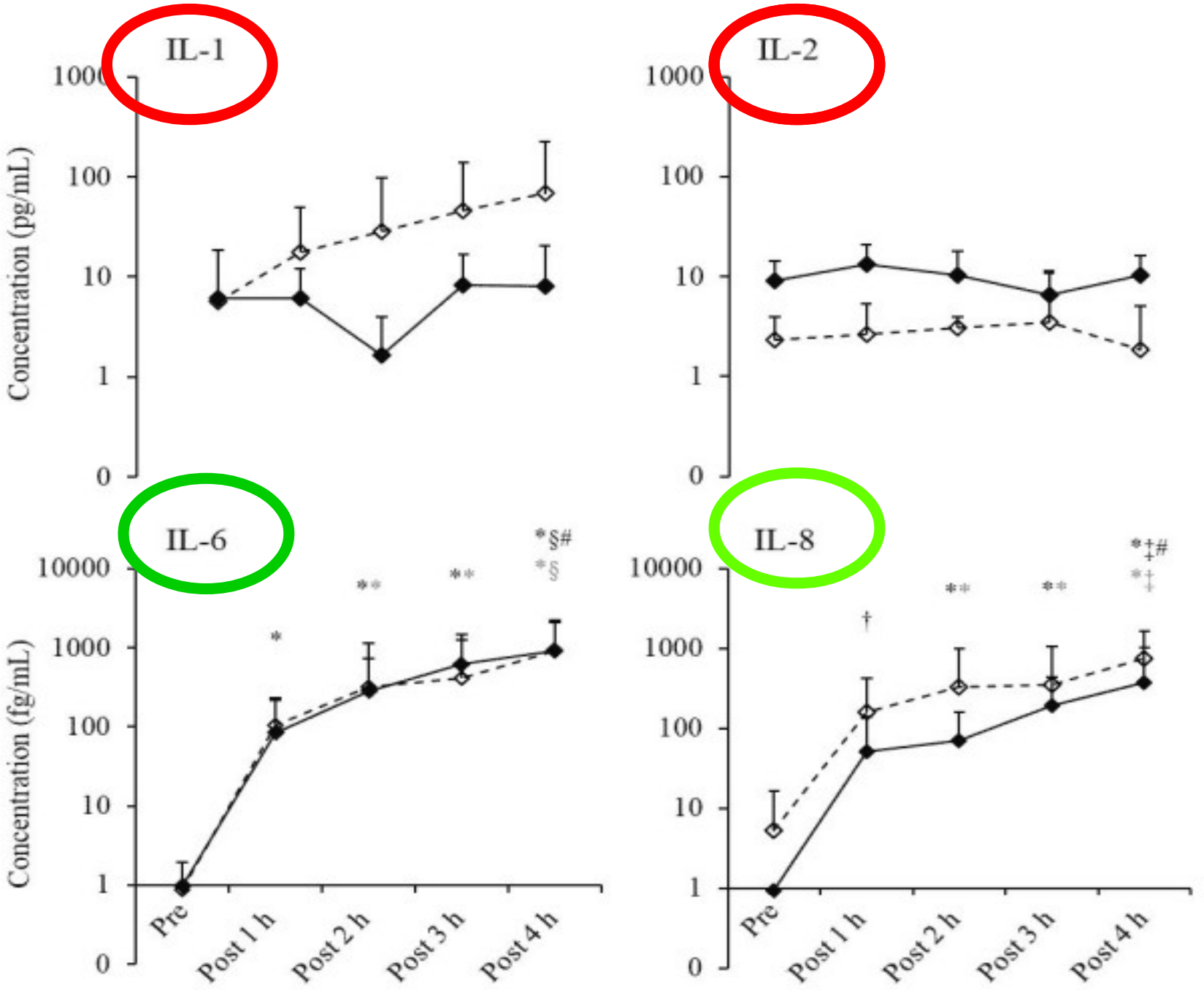
Use generous amount of coupling ultrasound gel.

How Does It Work?

- Neovascularization or new blood supply[1,3]
  - More blood = more oxygen = better healing
- Stimulates fibroblasts for connective tissue healing[1,3]
  - Tendon, ligament, fascia

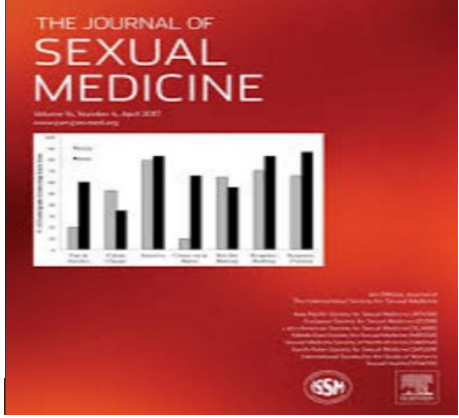





IL-1
IL-2
IL-6
IL-8
Concentration (pg/mL)
Concentration (fg/mL)
1000
100
10
1
0
10000
Pre
Post 1 h
Post 2 h
Post 3 h
Post 4 h

Effects of Low-Intensity Extracorporeal Shockwave Therapy on Erectile Dysfunction: A Systematic Review and Meta-Analysis.

Clavijo RI[1], Kohn TP[2], Kohn JR[2], Ramasamy R[3].



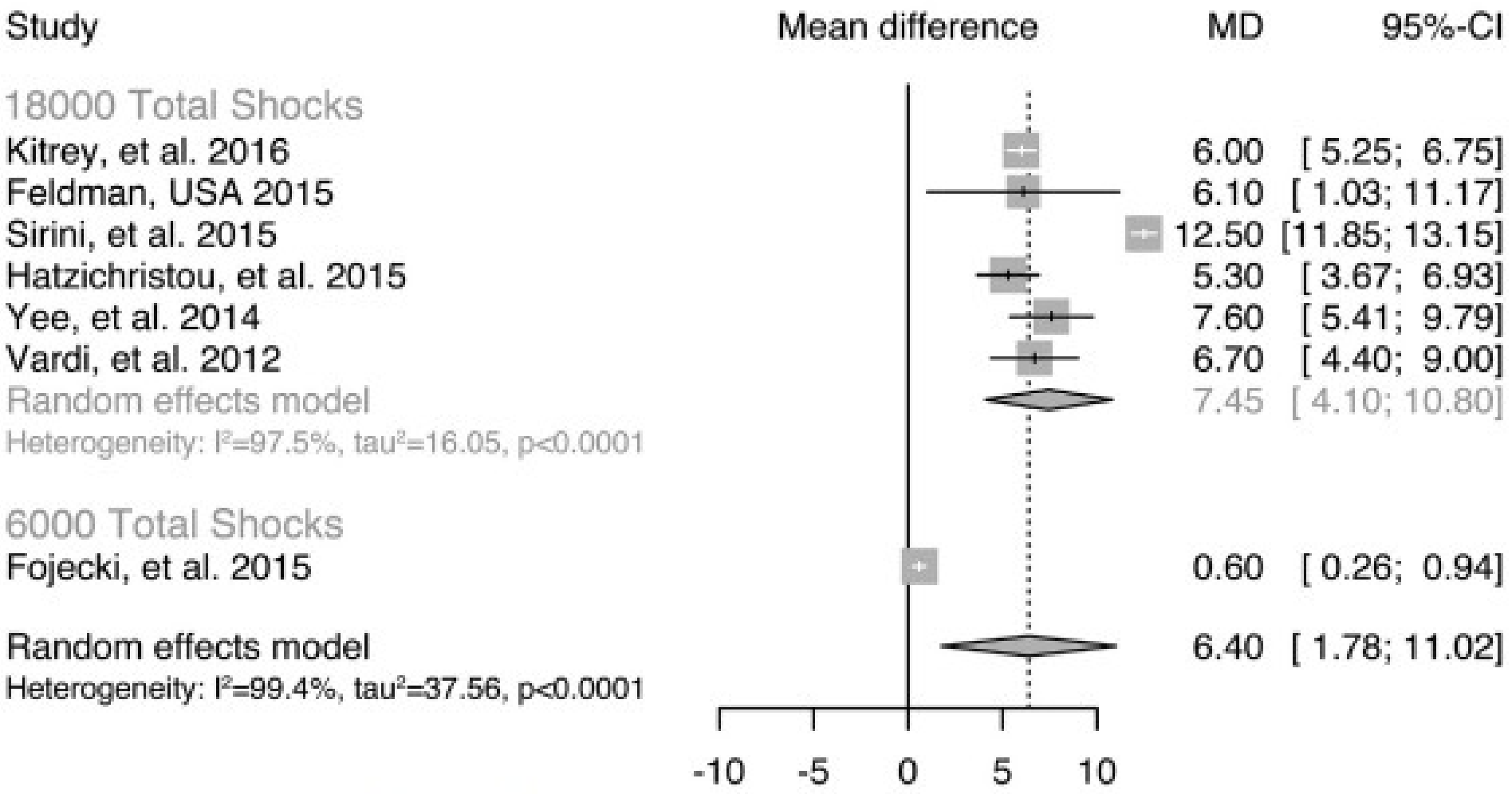


Figure 3. Sub-analyses by total treatment shocks.

Effects of Low-Intensity Extracorporeal Shockwave Therapy on Erectile Dysfunction: A Systematic Review and Meta-Analysis.

Clavijo RI[1], Kohn TP[2], Kohn JR[2], Ramasamy R[3].

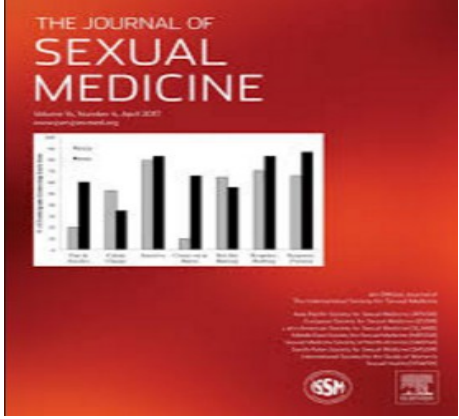


Table 2. Meta-regression by age and total shock energy

Meta-regression	Slope	Lower CI	Upper CI	Q	*P* value
Control arm					
Duration of follow-up	−0.01	−0.07	0.06	0.080	.78
Age (y)	−0.04	−0.37	0.30	0.05	.83
Baseline IIEF-EF score	0.15	−0.31	0.60	0.39	.53
Treatment arm					
Duration of follow-up	−0.05	−0.36	0.26	0.10	.75
Age (y)	−0.41	−0.95	0.14	2.16	.14
Baseline IIEF-EF score	−0.37	−2.80	2.07	0.09	.77

IIEF-EF = International Index of Erectile Function erectile function domain.

Problemi nella standardizzazione degli studi

Diverse macchine utilizzate:piezoelettriche, elettromagnetiche,elettroidrauliche

Diversi schemi terapeutici

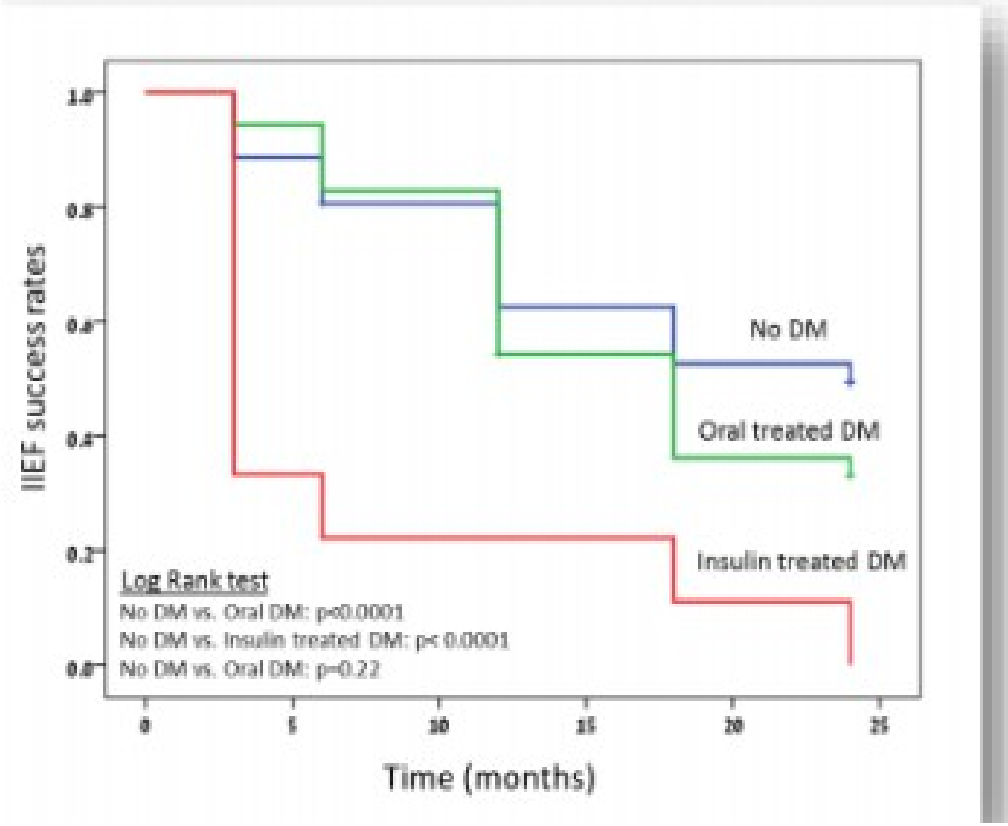
Diverso numero di colpi

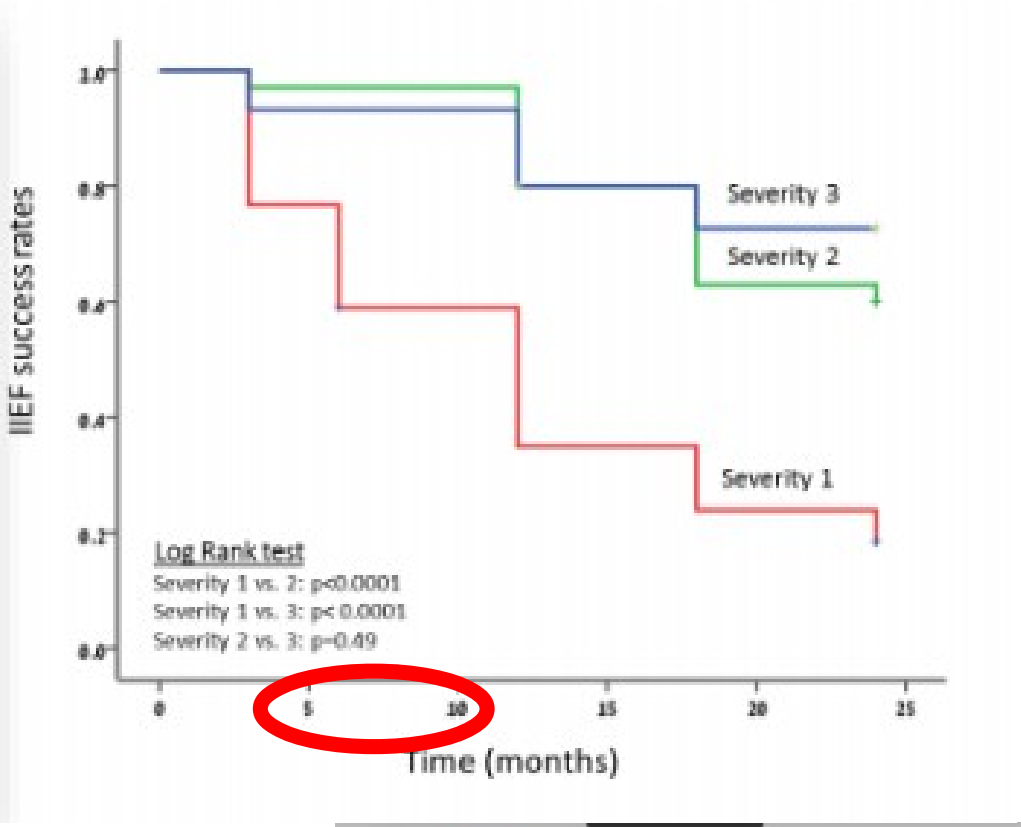
Diversa potenza

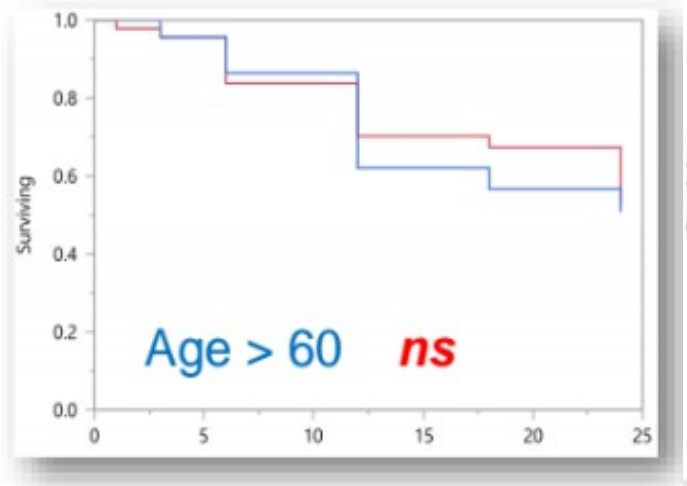
Who are the patients who will benefit from List

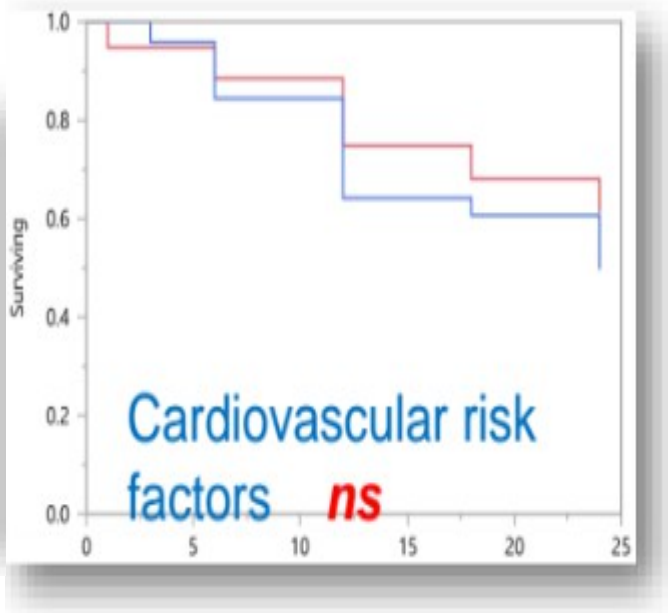
- Vasculogenic patients (vasculogenic background including diabetics)
- PDE5i Responder
- PDE5i Non responders need to have at least a certain erectile response and a short time of non responsiveness.

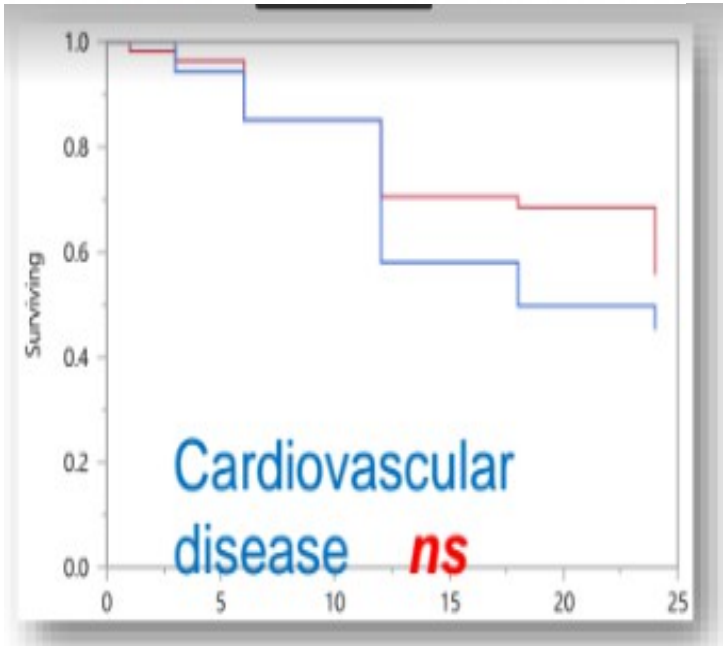
FOR HOW LONG DOES THE SW EFFECT LAST?


IIEF success rates
No DM
Oral treated DM
Insulin treated DM
Log Rank test
No DM vs. Oral DM: p<0.0001
No DM vs. Insulin treated DM: p< 0.0001
No DM vs. Oral DM: p=0.22
Time (months)


IIEF success rates
Severity 3
Severity 2
Severity 1
Log Rank test
Severity 1 vs. 2: p<0.0001
Severity 1 vs. 3: p< 0.0001
Severity 2 vs. 3: p=0.49
Time (months)

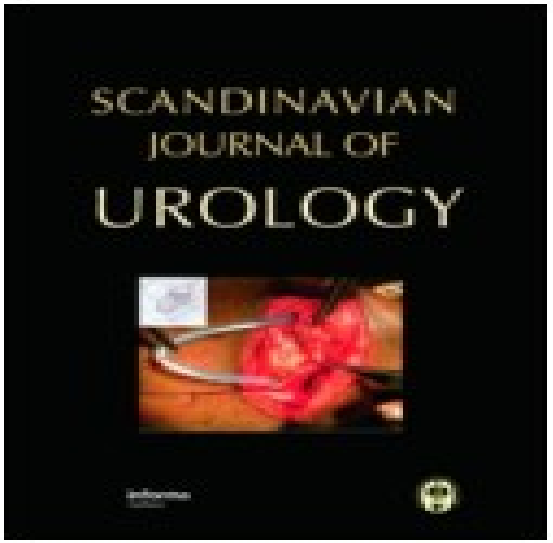

Surviving
Age > 60 ns


Surviving
Cardiovascular risk factors ns


Surviving
Cardiovascular disease ns

Low-intensity extracorporeal shockwave therapy in the treatment of postprostatectomy erectile dysfunction: a pilot study

Anders Frey, Jens Sønksen & Mikkel Fode



After Ralp ns

No Stratification based on iief 5

T1= 1 month ; T2 = 1 year

Table 1. Changes in erectile function (ED) categories.

Patient no.	ED category (baseline)	ED category (t1)	ED category (t2)
1	Severe	Severe	Severe
2	Severe	Severe	Severe
3	Severe	Mild to moderate	NA
4	Moderate	Mild to moderate	Moderate
5	Moderate	Moderate	Mild to moderate
6	Mild	Mild	Mild
7	Mild	No ED	No ED
8	Severe	Severe	Severe
9	Severe	Moderate	Moderate
10	Moderate	Moderate	Moderate
11	Moderate	Moderate	Severe
12	Moderate	Mild to moderate	No ED
13	Mild to moderate	Mild	Mild
14	Mild	Mild	Mild
15	Mild	Mild	Mild
16	Moderate	Mild to moderate	Moderate

NA = not applicable.

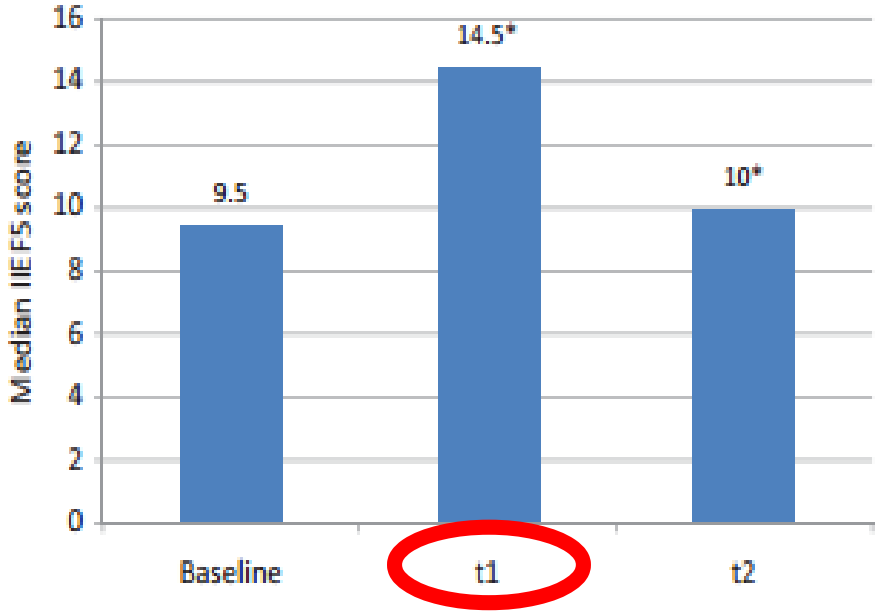


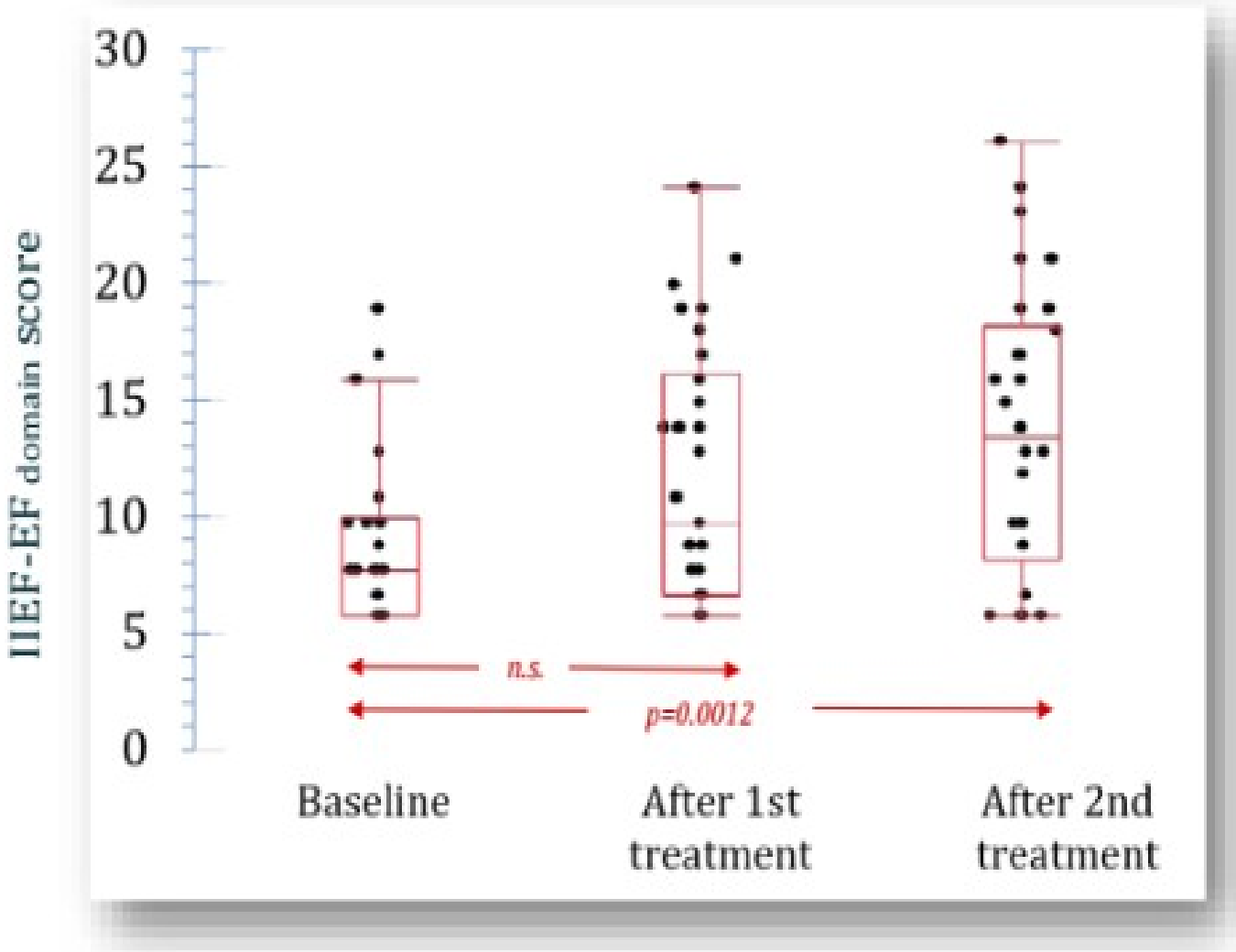
Figure 1. Median changes in International Index of Erectile Function-5 (IIEF5) scores. *$p < 0.05$.

Second round

Does an additional series of LIST can improve the results for the patients that failed or partially responded to the first round of therapy?

A "Second round" protocol is **effective in approximately half the patients** who responded poorly to the standard one.

Improvement of IIEF-EF score after 1st & 2nd treatment



Vardi Y et al. EAU 2014 abstract 604

SIA

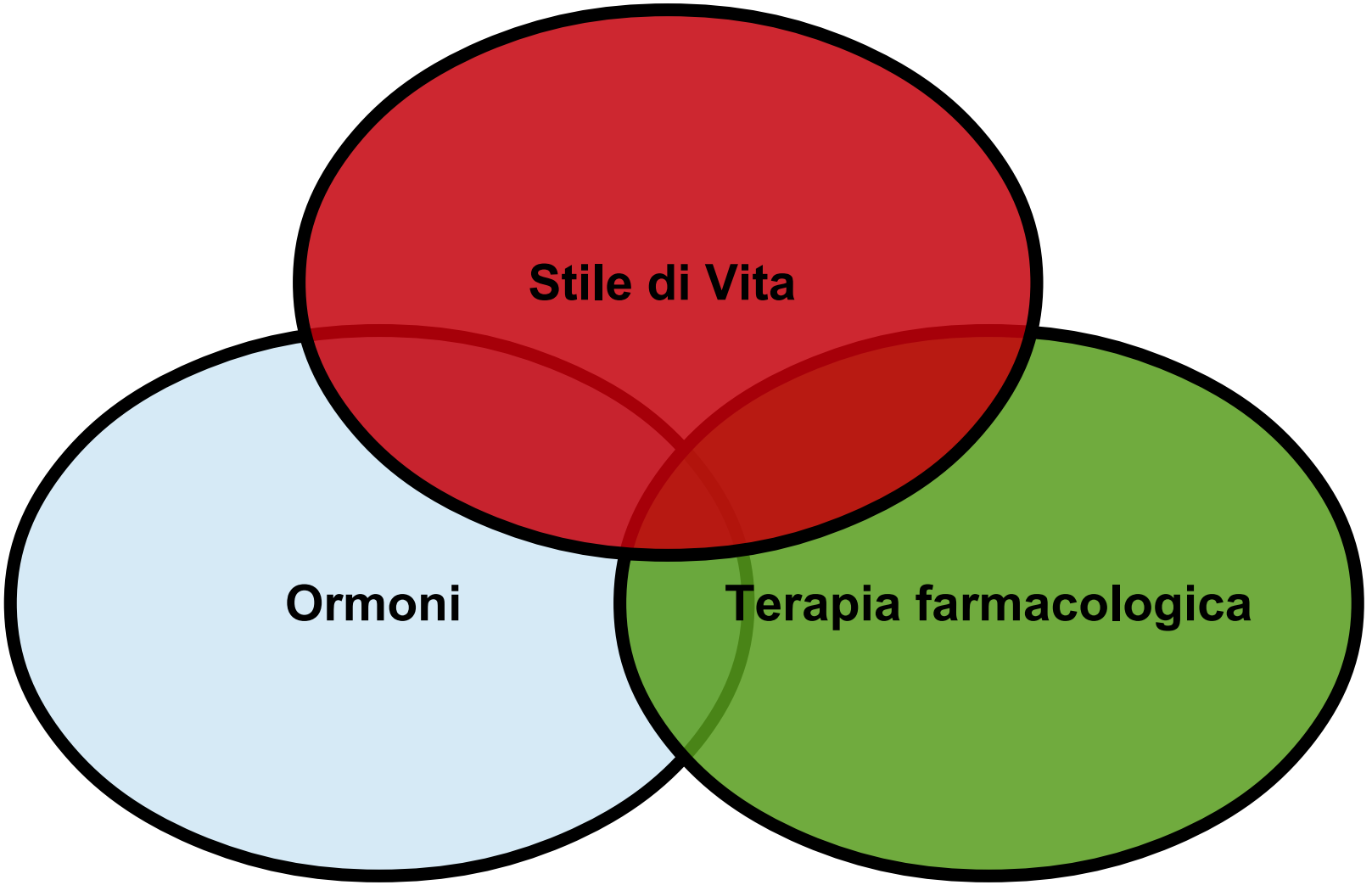
Società Italiana
di Andrologia

“Onde d’Urto a bassa intensità: la nuova frontiera della terapia della DE”

Responsabili del progetto

Fabrizio Palumbo
Alessandro Palmieri

Terapia di associazione


Stile di Vita
Ormoni
Terapia farmacologica

TESTOSTERONE E PCa: LA VISIONE TRADIZIONALE

- ↑ T causa Pca
- ↓ T protegge da Pca

- Rapido incremento del T causa una rapida crescita del Pca *"è come buttare benzina sul fuoco"*

TESTOSTERONE E PCa: LA VISIONE TRADIZIONALE

- ↑ T causa Pca
- ↓ T protegge da Pca

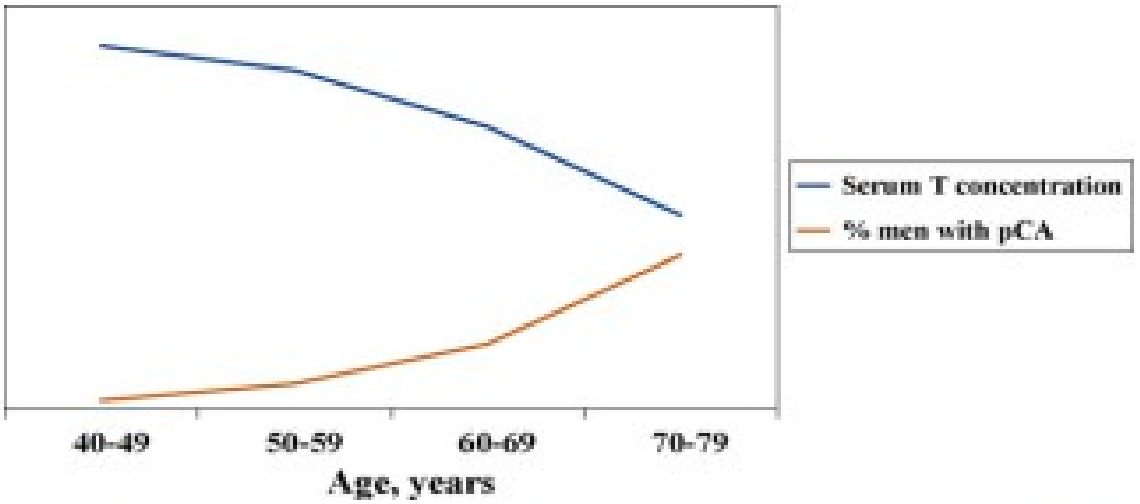


Fig. 1 – Prostate cancer prevalence and testosterone levels with ageing. pCA: prostate cancer, T: testosterone.

REVIEW ARTICLE 2004

Risk of testosterone replacement therapy and raccomandation for monitoring

The New England Journal of Medicine

Numero di articoli (1985-2004) che mostrano una preoccupante relazione tra T e PCa

QUALI SONO LE EVIDENZE ATTUALI DELLA LETTERATURA ?

NESSUNO

T and Pca in Placebo Arm of REDUCE TRIAL

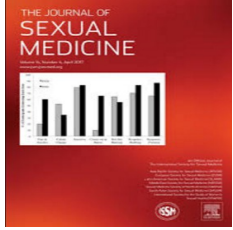
Muller et al, European Urology 2012

- 3255 pazienti
- Dosaggio basale del T e DHT
- Risultati: nessuna associazione tra Pca e T/DHT
- Uomini con elevato T non hanno un aumentato rischio di PCa

No increase in Pca rates with T therapy in RCTs

Cui et al, Pros. Canc. Dis. 2014

- Metanalisi di 22 RCTs
- 2351 pazienti
- Risultati: nessuna differenza di incidenza di Pca tra gli uomini trattati con T Vs Placebo

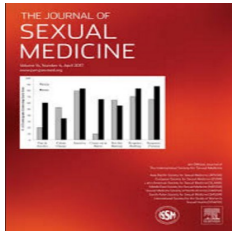


SEXUAL MEDICINE REVIEWS

Testosterone Therapy Among Prostate Cancer Survivors

Taylor M. Nguyen[1] and Alexander W. Pastuszak, MD, PhD[2,3]

Conclusion: Despite the historical reluctance toward the use of testosterone therapy in men with a history of prostate cancer, modern evidence suggests that testosterone replacement is a safe and effective treatment option for hypogonadal men with non–high-risk prostate cancer. Additional work to definitively demonstrate the efficacy and safety of testosterone therapy in men with prostate cancer is needed, and persistent vigilance and surveillance of treated men remains necessary.



Testosterone replacement therapy following the diagnosis of prostate cancer: outcomes and utilization trends.

Kaplan AL[1], Trinh QD, Sun M, Carter SC, Nguyen PL, Shih YC, Marks LS, Hu JC.

CONCLUSIONS: In this population-based observational study of testosterone replacement therapy in men with a history of prostate cancer, treatment was not associated with increased overall or cancer-specific mortality. These findings suggest testosterone replacement therapy may be considered in men with a history of prostate cancer, but confirmatory prospective studies are needed.

Testosterone Replacement Therapy in Patients with Prostate Cancer After Radical Prostatectomy

Alexander W. Pastuszak,* Amy M. Pearlman,* Win Shun Lai,* Guilherme Godoy,* Kumaran Sathyamoorthy,* Joceline S. Liu,* Brian J. Miles,* Larry I. Lipshultz† and Mohit Khera‡,§

THE JOURNAL of UROLOGY®
Official Journal of the American Urological Association

TRT results in increases in serum T levels, with a small but significant rise in PSA and a lower BCR rate in treated men

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European Association of Urology

Testosterone levels and prostate cancer prognosis: A systematic review and meta-analysis

Claps, Berruti et all

In early PC, serum testosterone level was not prognostic in terms of overall survival (OS) and biochemical recurrence (BCR)

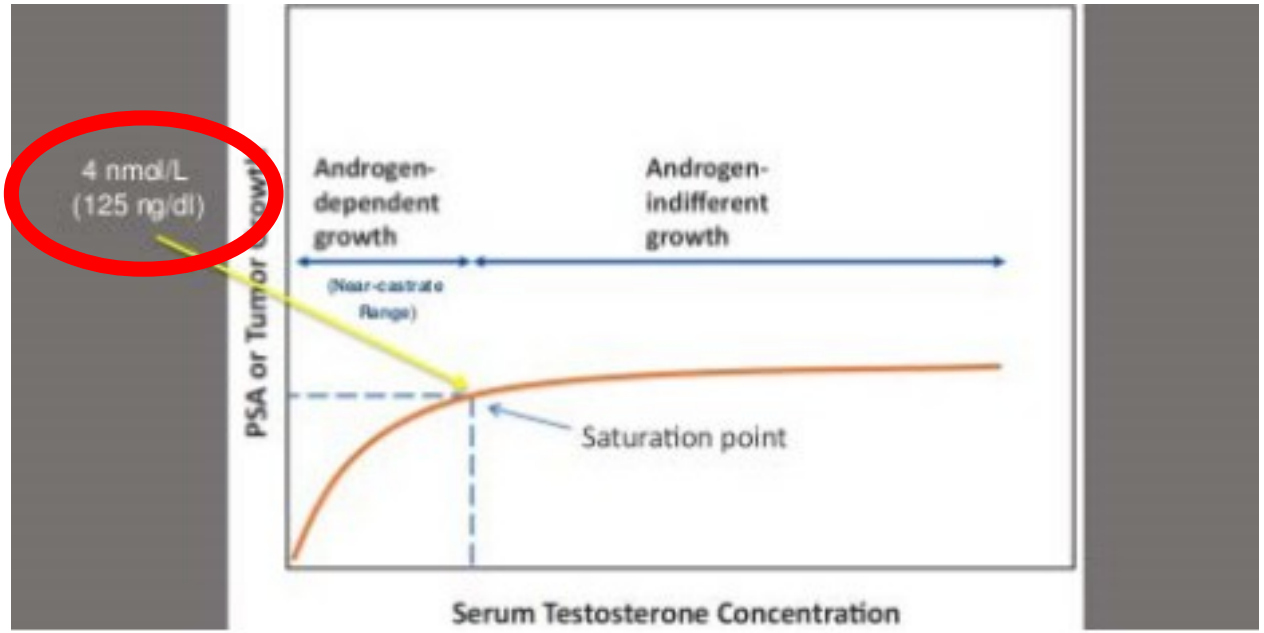
During ADT, lower levels were associated with a reduced risk of progression and death

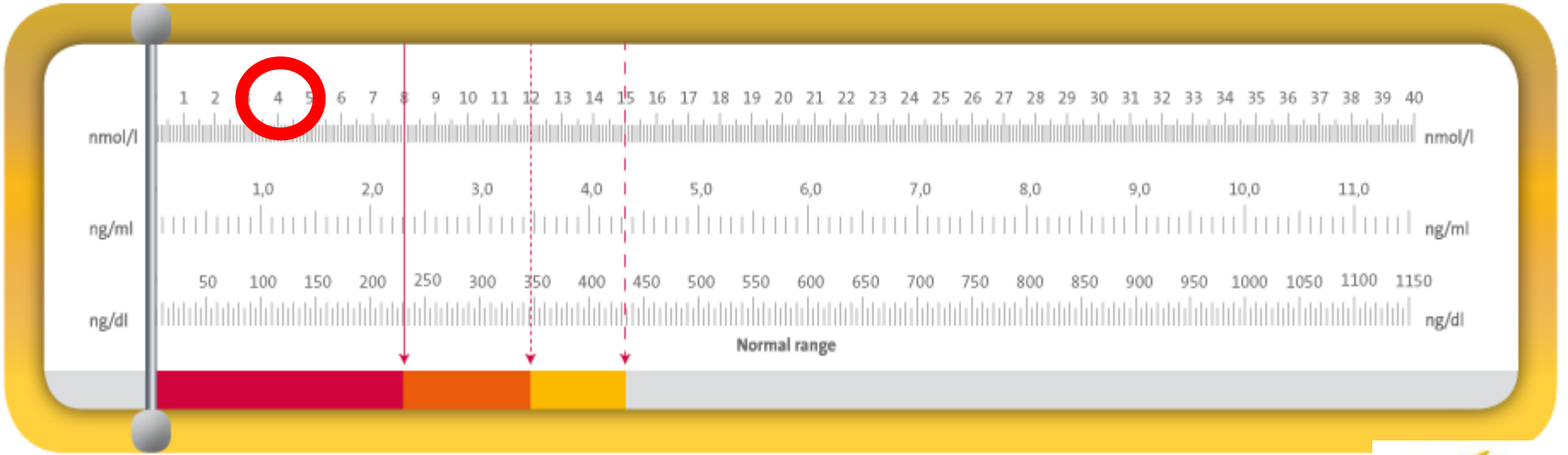
In CRPC patients, higher testosterone levels predicted a reduced risk of progression

Men who receive testosterone therapy after treatment for localized PC do not suffer from higher rates of recurrence or have worse outcomes

Saturation Model

Morgentaler, Urol Clin. NA 34:555, 2007





NEBIDO
Testosterone Undecanoate

Changes in sex hormone levels after radical prostatectomy: Results of a longitudinal cohort study

MAURO GACCI[1], NICOLA TOSI[1], GIANNI VITTORI[1], ANDREA MINERVINI[1], GIOVANNI CORONA[2], TOMMASO CAI[3], ANNA MARIA MORELLI[4], LINDA VIGNOZZI[4], SERGIO SERNI[1], MARIO MAGGI[4] and MARCO CARINI[1]

[1]Department of Urology, University of Florence, Florence; [2]Endocrinology Unit, Maggiore-Bellaria Hospital, Bologna; [3]Department of Urology, Santa Chiara Regional Hospital, Trento; [4]Department of Clinical Physiopathology, University of Florence, Florence, Italy

Received November 29, 2012; Accepted March 28, 2013

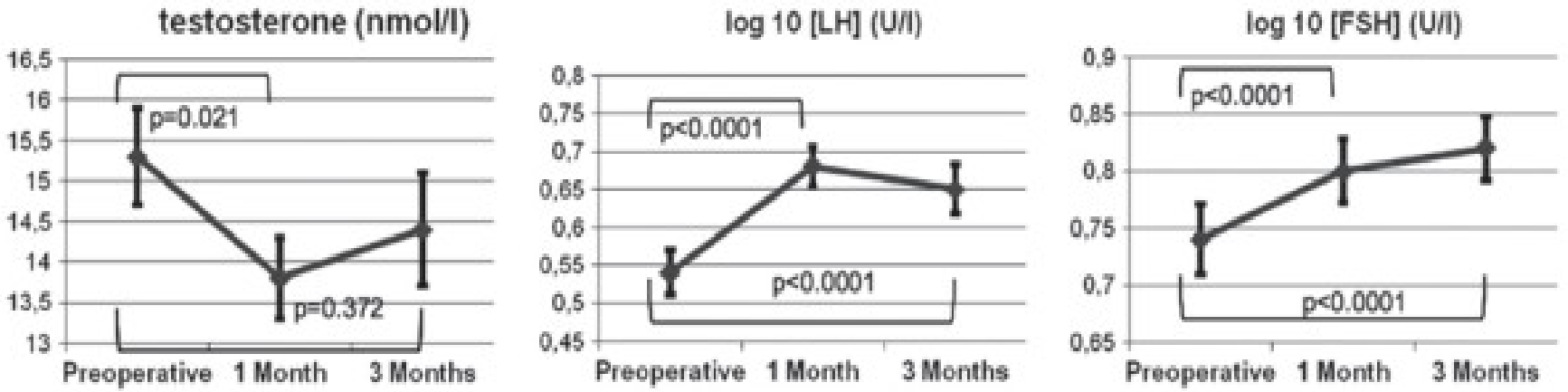


Figure 1. Comparisons of the serum hormone levels at baseline with those at 1 and 3 months from 92 PCa patients with complete data. Paired t-tests were used for Te (normally distributed, expressed as nmol/l) and logarithmically transformed LH and FSH (not normally distributed, expressed as U/l). Data are expressed as the mean ± standard error of the mean. LH, luteinizing hormone; FSH, follicle-stimulating hormone; Te, testosterone; PCa, prostate cancer.

In the present study, patients developed compensated ***hypergonadotropic hypogonadism 3 months after RP***

Perche dosare il testosterone dopo prostatectomia ?

1) Paziente ipogonadico precedentemente alla chirurgia o al trattamento locale

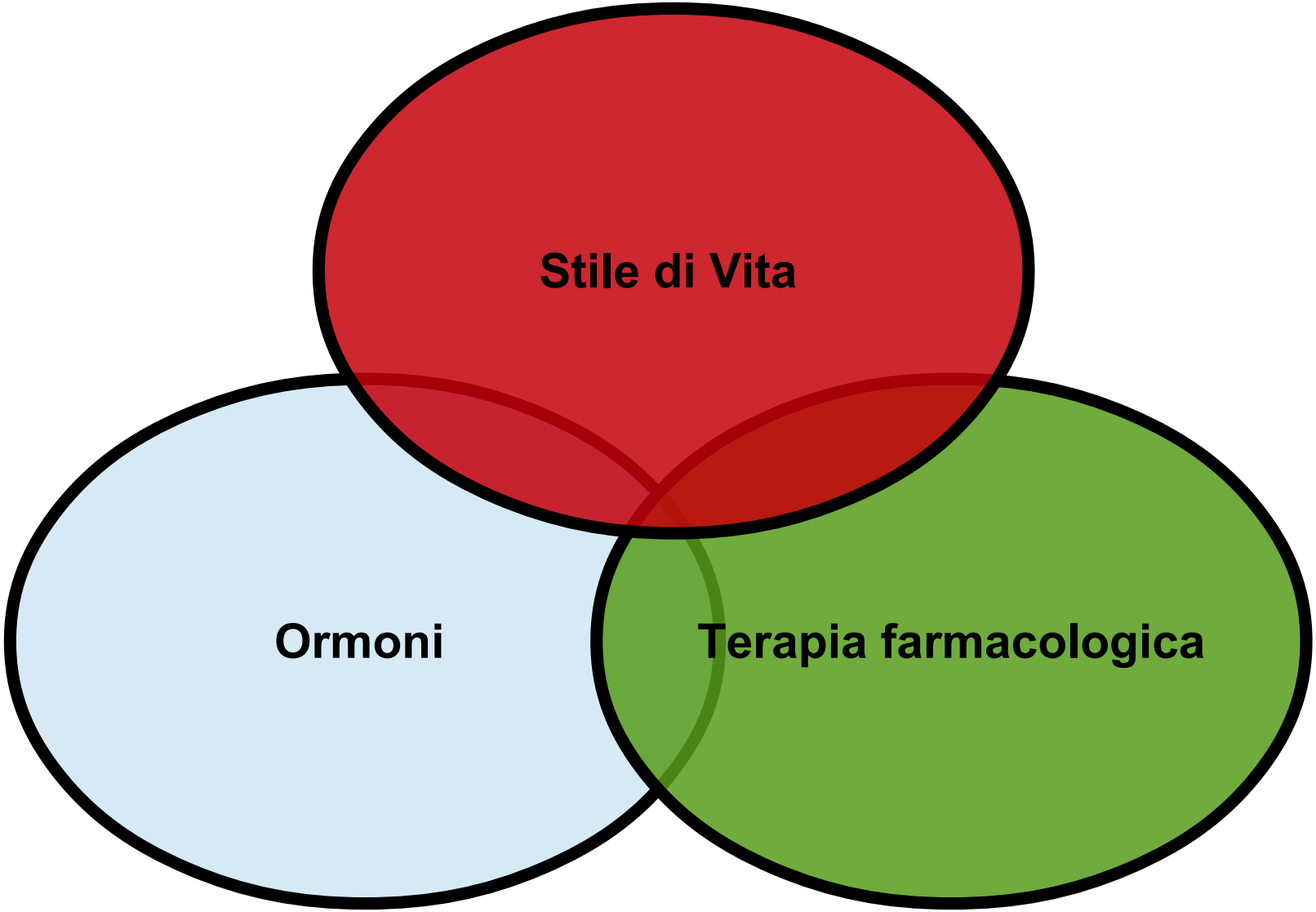
2) Perchè sono dimostrate correlazioni tra prostatectomia, radioterapia ed ipogonadismo [1]

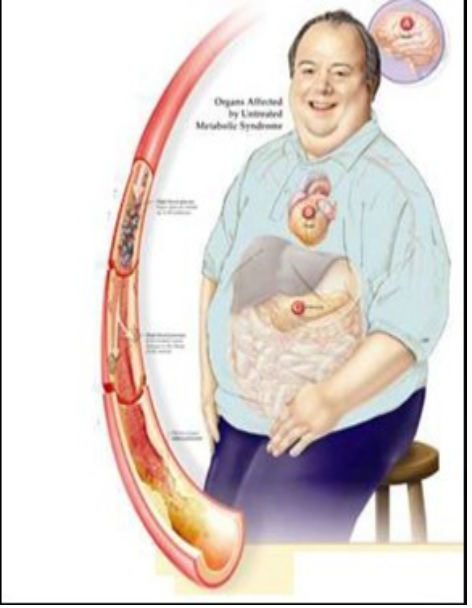
3)Migliorare la funzione erettile e l' azione dei pde 5 tramite eventuale T replacement

4)proteggere dalla sarcopenia, sindrome metabolica , demineralizzazione ossea, patologie cardiovascolari (sprt danno microvascolare), depressione e astenia [2]

*1) J sex med 2007.External beam radioterapy affects serum testosterone in patient with localized prostate cance*r

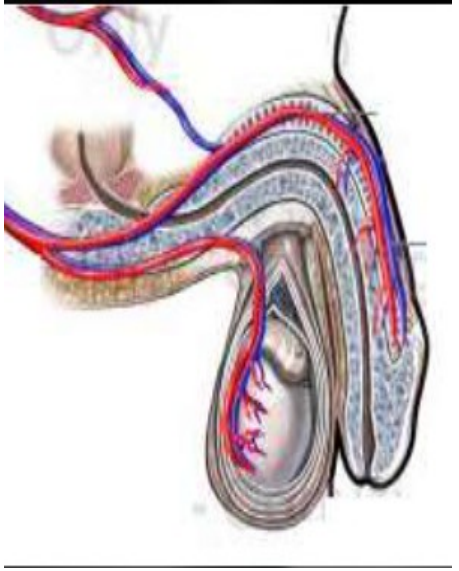
2)*Vignozzi L, Morelli A, Sarchielli E, Comeglio P, Filippi S, et al. Testosterone protects from metabolic syndrome-associated prostate inflammation: an experimental study in rabbit. J*


Stile di Vita
Ormoni
Terapia farmacologica



Sindrome metabolica

Spesso l'approccio alla disfunzione erettile è prettamente farmacologico escludendo esami di primo e secondo livello

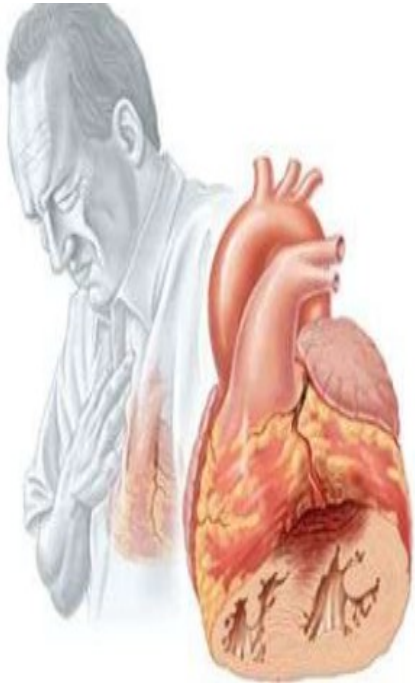


Disfunzione erettile

Iperplasia prostatica

E' necessario al contrario capire se la disfunzione erettile e' un sintomo di una disfunzione cardiovascolare

Danno Vascolare



JAMA®

Online article and related content current as of January 17, 2010.

Erectile Dysfunction and Subsequent Cardiovascular Disease

Ian M. Thompson; Catherine M. Tangen; Phyllis J. Goodman; et al.

JAMA. 2005;294(23):2996-3002 (doi:10.1001/jama.294.23.2996)

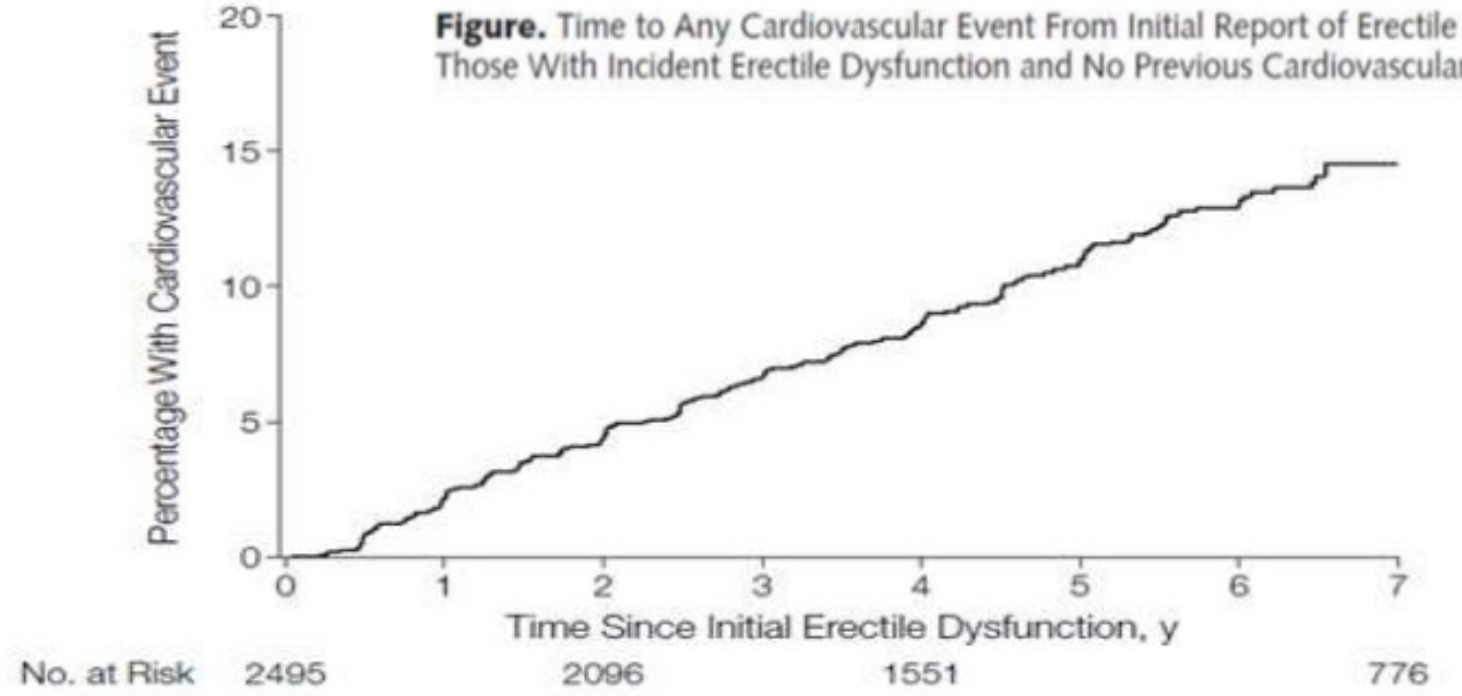


Figure. Time to Any Cardiovascular Event From Initial Report of Erectile Dysfunction for Those With Incident Erectile Dysfunction and No Previous Cardiovascular Event

t risk, n = 2495; number of cardiovascular events, 255; 5-year estimate of cardiovascular events, 11%.

The presence of moderate-severe ED is associated with a significant risk to develop ED in the next 10 years

Table 4 – Recommendations for the treatment of erectile dysfunction (ED)

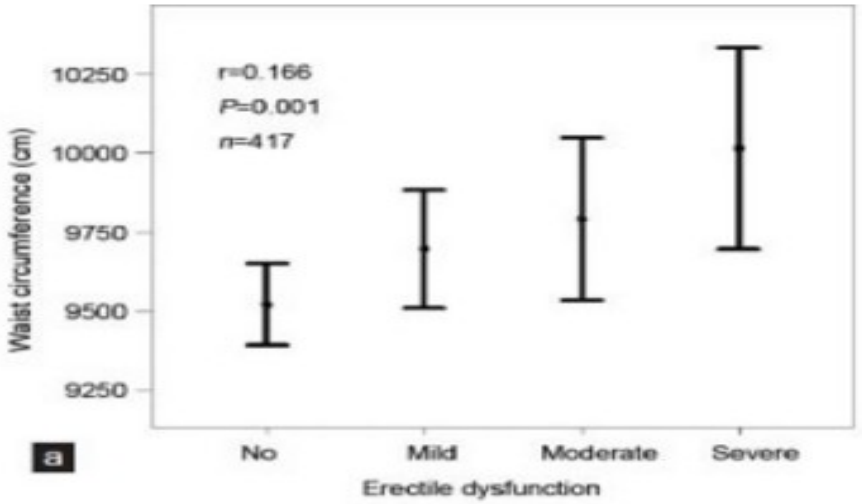
Recommendations	LE	GR
Lifestyle changes and risk factor modification must precede or accompany ED treatment.	1b	A
Pro-erectile treatments must be given at the earliest opportunity after radical prostatectomy.	1b	A
If a curable cause of ED is found, treat the cause first.	1b	B
PDE5-Is are first-line therapy.	1a	A
Daily administration of PDE5-Is may improve results and restore erectile function.	1b	A
Inadequate/incorrect prescription and poor patient education are the main causes of a lack of response to PDE5-Is.	3	B
Testosterone replacement restores efficacy in hypogonadic nonresponders to PDE5-Is.	1b	B
Apomorphine can be used in mild to moderate ED, psychogenic ED, or in patients with contraindications to PDE5-Is.	1b	B
A vacuum constriction device can be used in patients with stable relationship.	4	C
Intracavernous injection is second-line therapy.	1b	B
Penile implant is third-line therapy.	4	C

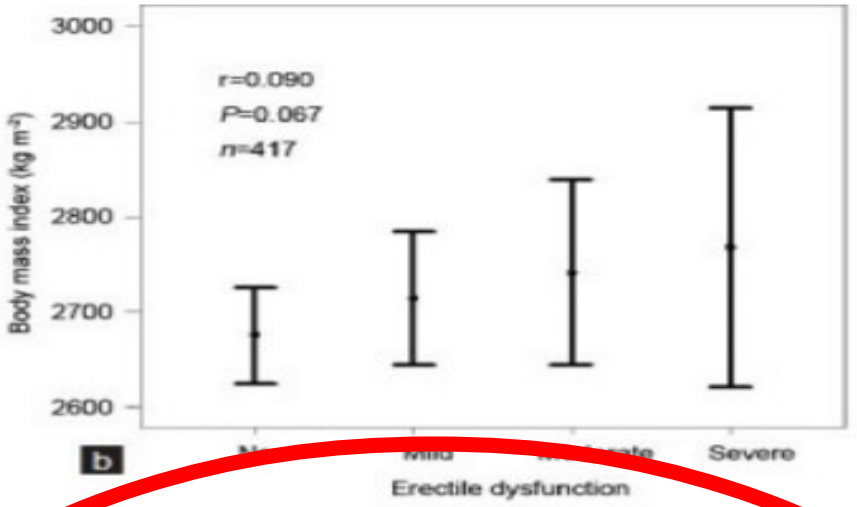
LE = level of evidence; GR = grade of recommendation; PDE5-I = phosphodiesterase type 5 inhibitor.

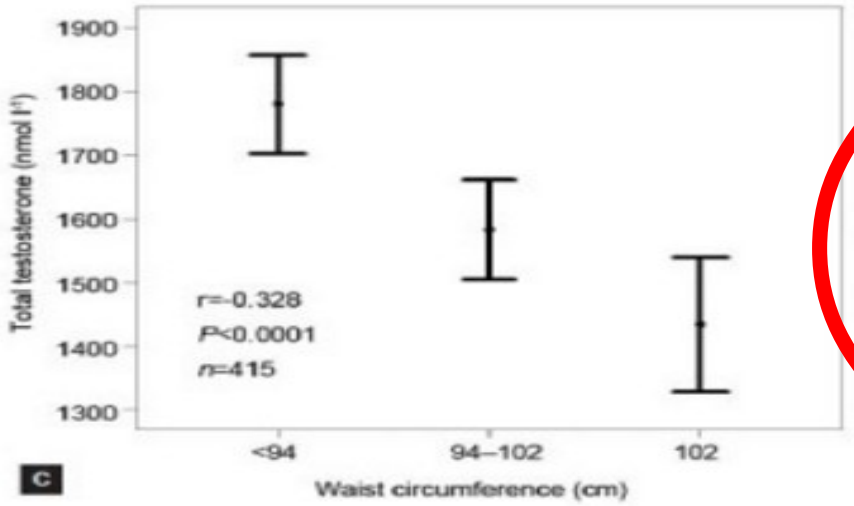
Asian Journal of Andrology

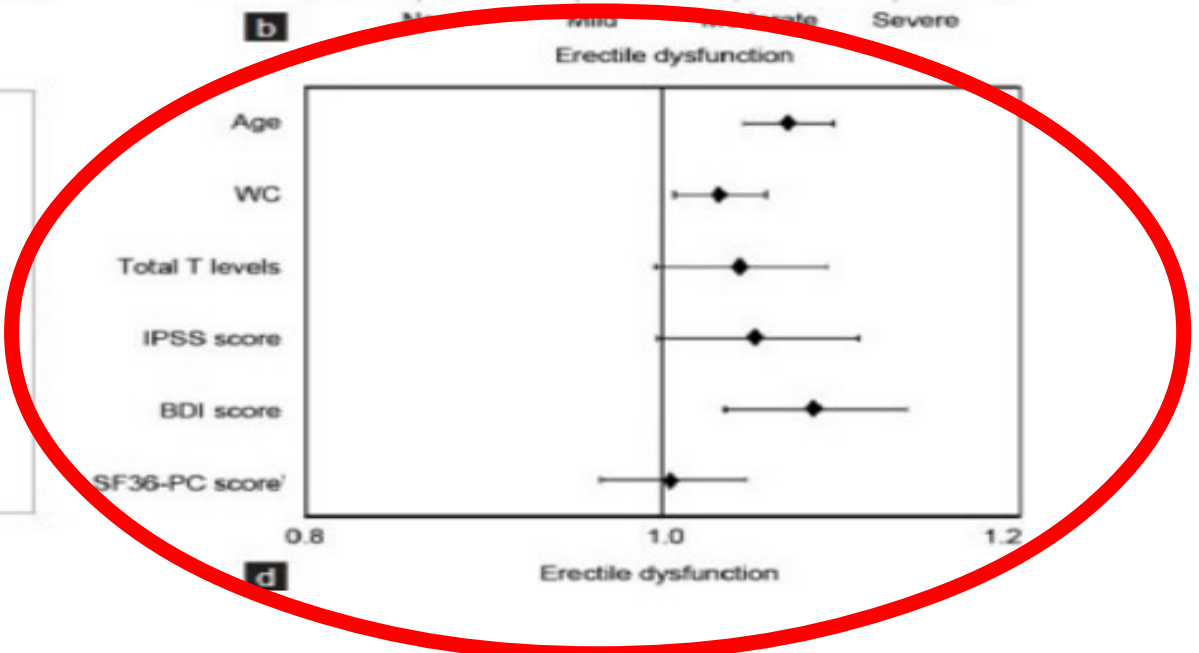
Erectile dysfunction and central obesity: an Italian perspective

Giovanni Corona,[1] Giulia Rastrelli,[2] Sandra Filippi,[2] Linda Vignozzi,[2] Edoardo Mannucci,[3] and Mario Maggi[2]









ORIGINAL ARTICLE
Mediterranean diet improves erectile function in subjects with the metabolic syndrome

K Esposito[1], M Ciotola[1], F Giugliano[2], M De Sio[2], G Giugliano[3], M D'Armiento[2] and D Giugliano[1]

[1]*Division of Metabolic Diseases, University of Naples SUN, Naples, Italy;* [2]*Division of Urology, University of Naples SUN, Naples, Italy and* [3]*Plastic and Reconstructive Surgery, University of Rome 'La Sapienza', Rome, Italy*

Table 4 Changes in IIEF score between the two groups

	Mediterranean diet	*Control diet*	*P-value*
Basal	14.4±3.8	14.9±3.7	NS
2 years	18.1±4	15.2±3.5	<0.01
Difference in mean change	3 (0.6–5.2)[a]		=0.01

[a]95% confidence intervals.
NS-Not Significant.

Table 3 Changes in assessed variables after 2 years

Variable	*Mediterranean diet (n=35)* Mean change	*Control diet (n=30)* Mean change	*P-value*
Body mass index (kg/m^2)	−0.3±0.1	−0.1±0.2	NS
Waist circumference (cm)	−1±0.5	0±0.5	NS
Plasma glucose (mg/dl)	−5±3	−1±1	<0.05
Serum insulin (μU/ml)	−2±1.9	0±0.2	<0.05
Serum lipids (mg/dl)			
Total cholesterol	−5±4	−2±2	NS
HDL-cholesterol	+3±1	0±0.5	<0.05
LDL-cholesterol	−10±4	1±2	<0.02
Triglycerides	−16±8	−2±2	<0.05
Blood pressure, mmHg			
Systolic	−4±1	0±	<0.05
Diastolic	−2±1	−1±1	NS
Endothelial function score	+1.6±0.6	+0.1±0.1	<0.01
CRP (mg/l)	−0.9±0.4	−0.1±0.1	<0.01

NS-Not Significant.

REVIEW

Physical activity and erectile dysfunction: meta-analysis of population-based studies

JYW Cheng, EML Ng, JSN Ko and RYL Chen

Department of Psychiatry, Li Ka Shing Faculty of Medicine, University of Hong Kong, Hong Kong

International Journal of Impotence Research
The Journal of Sexual Medicine

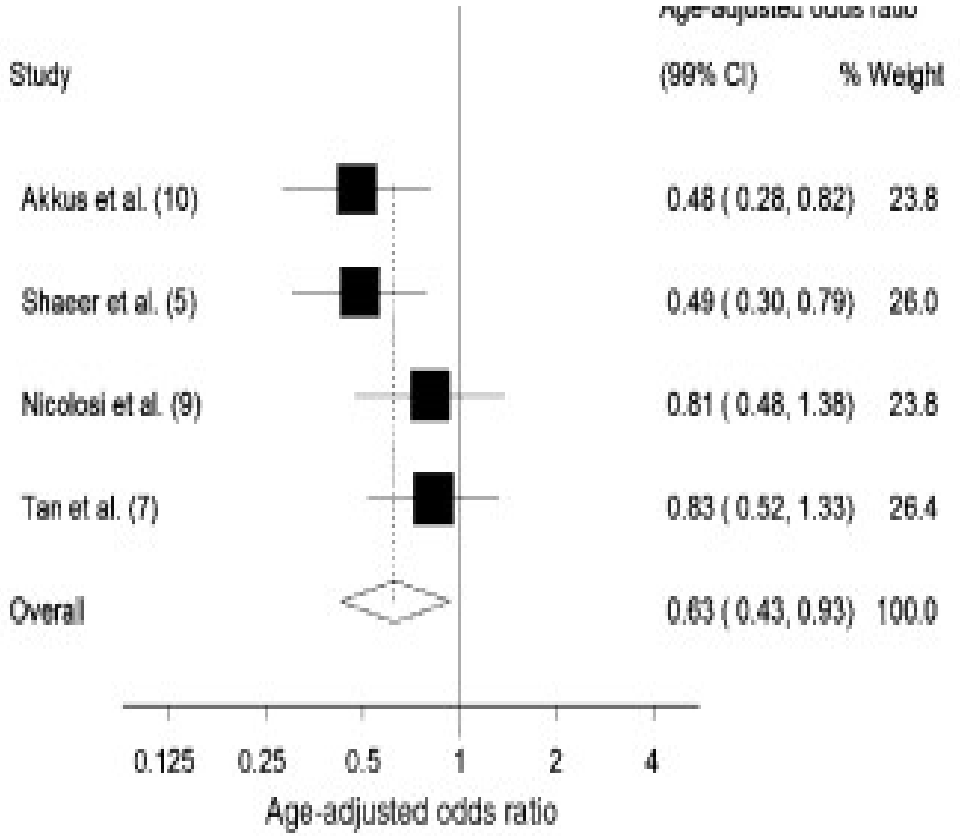


Figure 2 Risk of ED for moderate physical activity. Number of variables adjusted for in parentheses.

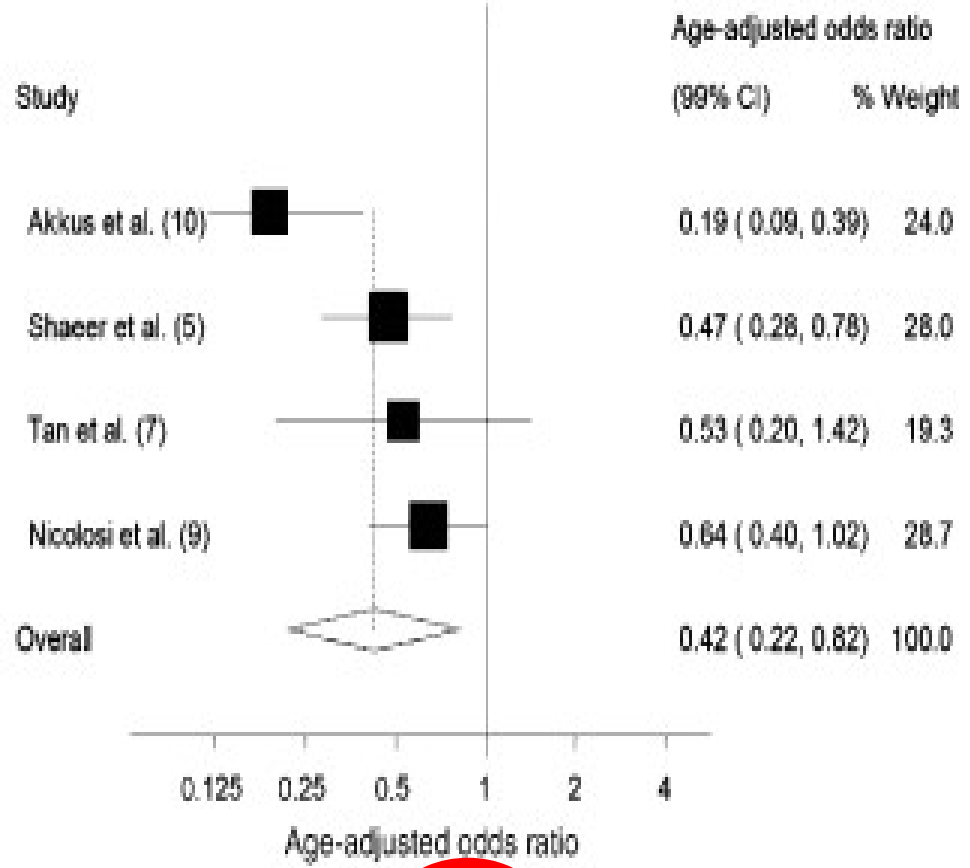


Figure 3 Risk of ED for high physical activity. Number of variables adjusted for in parentheses.

Sexual health ,adherence to Mediterranean diet, body weight, physical activity, mental state: four factors strongly correlated with each other

Pier Andrea Della Camera, Mauro Gacci, Gianmartin Cito, Simone Morselli, Nicola Laruccia,Giovanni Tasso, Sergio Serni, Marco Carini,Alessandro Natali.

N.Pazienti= 67	
E.D.=32	N.E.D.=35

Parametri esclusione
Ipogonadismo
Malatttia cardiovascolare
Diabete
Iperlipidemia
Fumo
Chirurgia Pelvica
Malattie neurologiche

Sexual health ,adherence to Mediterranean diet, body weight, physical activity, mental state: four factors strongly correlated with each other

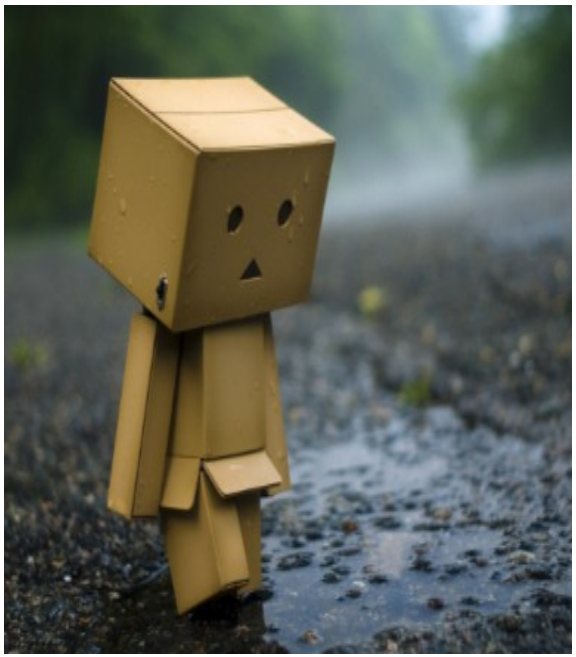
Pier Andrea Della Camera, Mauro Gacci, Gianmartin Cito, Simone Morselli, Nicola Laruccia,Giovanni Tasso, Sergio Serni, Marco Carini,Alessandro Natali.

	E.D. Vs N.E.D. ***T student***	***E.D. Vs N .E.D*** ***chi-square***
Physical Activity	p = 0.732	Yates = 0.866; O.D. = 1.4
Strenuos Physical Activity (>2520 met)	n.d.	P<0,001
Med Diet	p <0.0001	P <0.001 ; yates p <0.0049; or = 0.02
Bmi	P<0,001	n.d.
Hamilton	0.44;	Yates = 0.14; O.D. = 1.7

Sexual health ,adherence to Mediterranean diet, body weight, physical activity, mental state: four factors strongly correlated with each other

Pier Andrea Della Camera, Mauro Gacci, Gianmartin Cito, Simone Morselli, Nicola Laruccia,Giovanni Tasso, Sergio Serni, Marco Carini,Alessandro Natali.

Post Hoc Analysis



	Depressi vs Non Depressio T student	Depressi vs Non Depressio Chi square
Strenuos Physical Activity (>2520 met)	nd	P<0,05
Med diet	nd	P<0,05
Bmi	P<0,001	

Ultimo ritrovato della scienza