

Rehabilitation of Sexual Function after Treatment of Prostate Cancer

Luca Incrocci, M.D., Ph.D.

Erasmus MC-Daniel den Hoed Cancer Center

Rotterdam, The Netherlands



Rotterdam, 4th June 2010

Prostate Cancer (PCa)

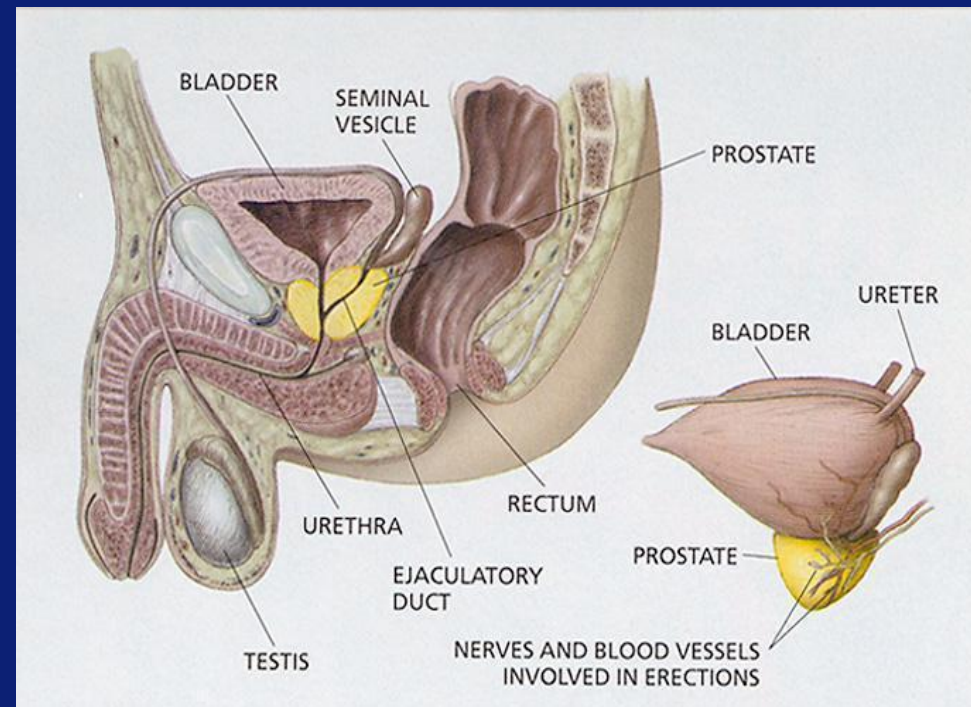
- PCa most frequent malignancy in men in Western countries
- More than 10,000 new cases in the NL in 2009
- Surgery (RP), external-beam radiotherapy (EBRT), brachytherapy (BT), W/see, hormones common treatment modalities

Erectile Dysfunction (ED) after RP

- Incidence: 40-100%
- Etiology: neurogenic (?)
- Onset: immediately

Stanford et al., JAMA 2000

Potosky et al., JNCI 2000



Phosphodiesterase Type 5 Inhibitors in Postprostatectomy Erectile Dysfunction: A Critical Analysis of the Basic Science Rationale and Clinical Application

Konstantinos Hatzimouratidis^{a,*}, Arthur L. Burnett^b, Dimitrios Hatzichristou^a, Andrew R. McCullough^c, Francesco Montorsi^d, John P. Mulhall^e

EUROPEAN UROLOGY 55 (2009) 334–347

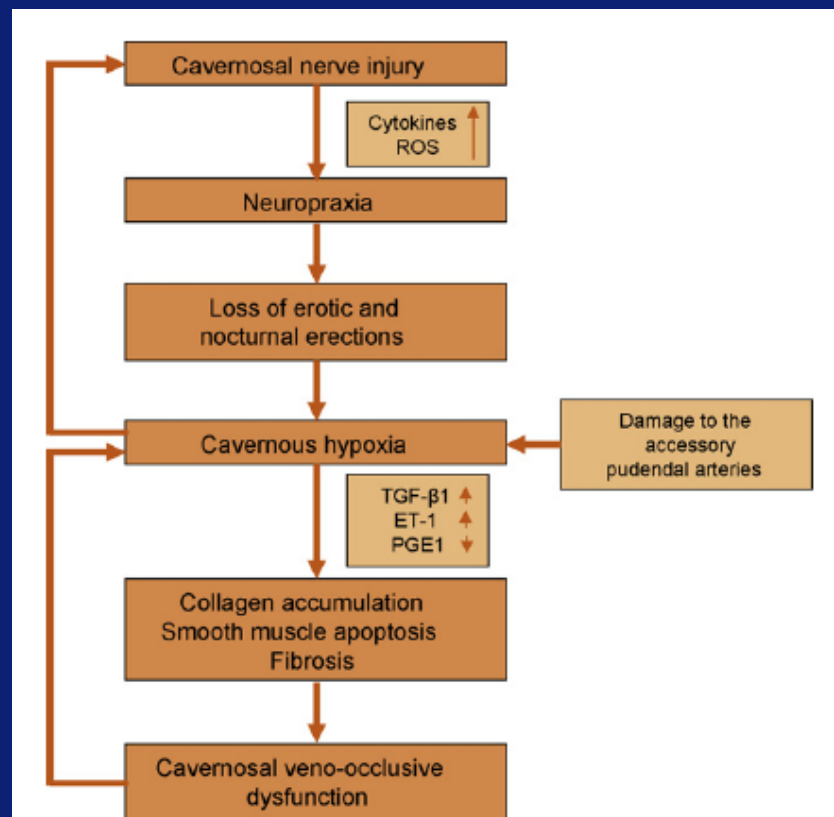
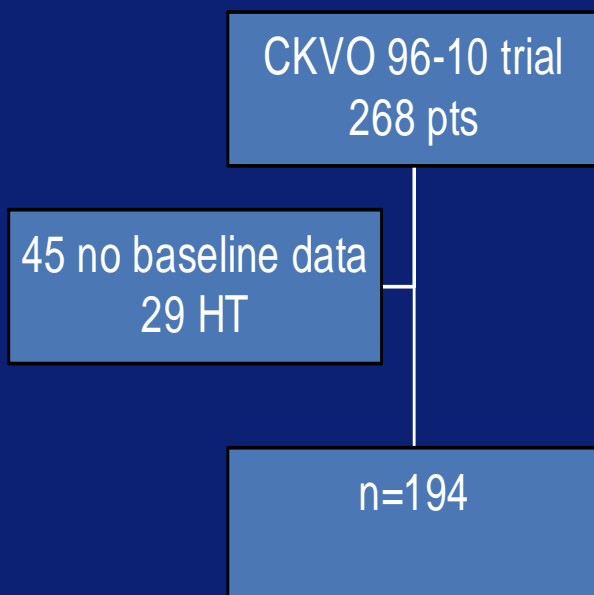


Fig. 1 – The vicious cycle of post-radical prostatectomy erectile dysfunction.

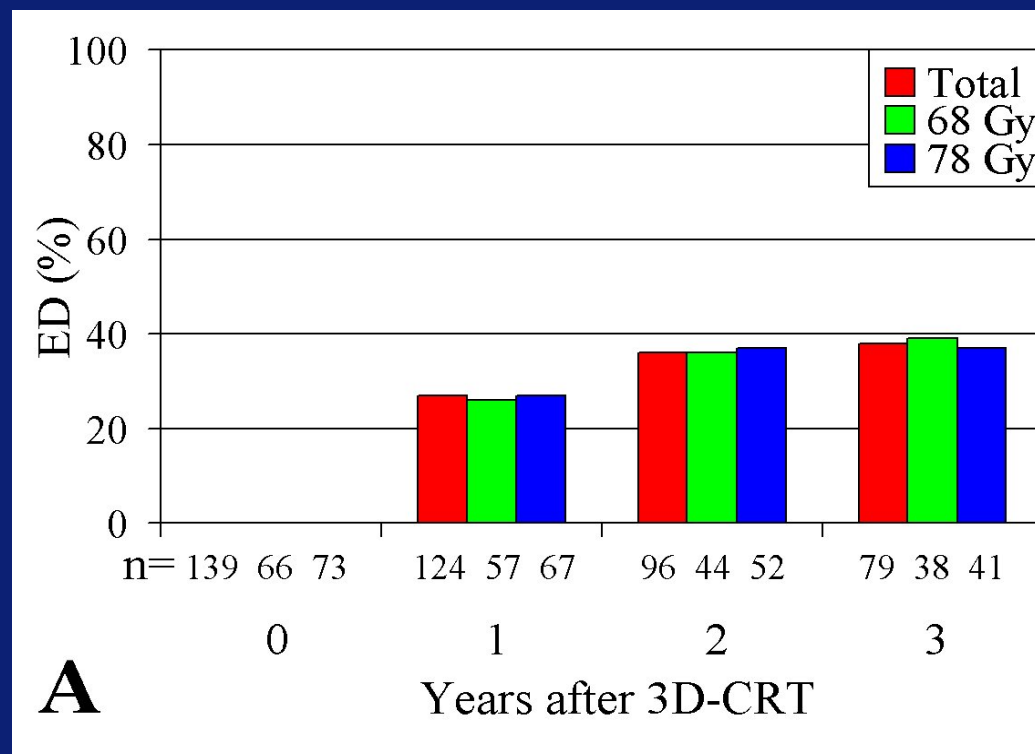
SEXUAL FUNCTION AFTER THREE-DIMENSIONAL CONFORMAL RADIOTHERAPY FOR PROSTATE CANCER: RESULTS FROM A DOSE-ESCALATION TRIAL

GERARD J. VAN DER WIELEN, M.D.,* WIM L.J. VAN PUTTEN, M.Sc.† AND
LUCA INCROCCI, M.D., Ph.D.*

Int. J. Radiation Oncology Biol. Phys., Vol. 68, No. 2, pp. 479–484, 2007



Questionnaire at baseline,
6 mos, 1, 2 & 3 yrs



Mechanisms of ED after EBRT/BT

Summary

- Arterial injury, arterial occlusion and cavernosal arterial insufficiency
- Endothelial dysfunction and structural alterations in corporal smooth muscles
- Distal pudendal arteries, crurae are at risk
- Vascular risk factors to be considered (DM, hypercholesterolemia, smoking...)

Van der Wielen et al., Radioth Oncol 2007

Phosphodiesterase Type 5 Inhibitors in Postprostatectomy Erectile Dysfunction: A Critical Analysis of the Basic Science Rationale and Clinical Application



Konstantinos Hatzimouratidis^{a,*}, Arthur L. Burnett^b, Dimitrios Hatzichristou^a, Andrew R. McCullough^c, Francesco Montorsi^d, John P. Mulhall^e

EUROPEAN UROLOGY 55 (2009) 334-347

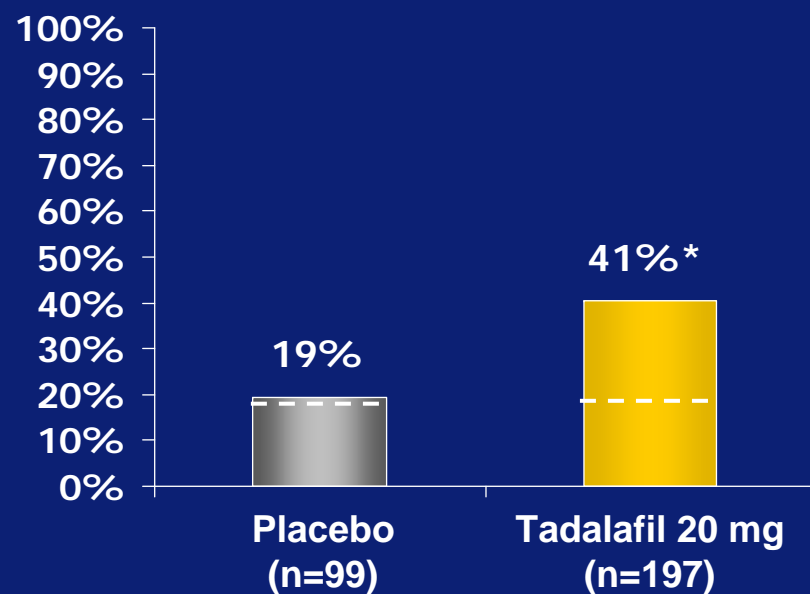
Table 3 – Clinical data on sildenafil treatment for post-radical prostatectomy erectile dysfunction

Study	N	Type of surgery (No.)	Efficacy tool	Response rates, %
Hong et al [72]	198	BNSRP (188) NNSRP (10)	EDITS score 1 or 2 in Q1 and Q2 (n = 80)	54–60 after 18–24 mo
Jarow et al [73]	77	Not specified	IIEF-5, satisfaction (single five-scale question)	Mean IIEF-5 score: 10.8 ± 9.2 Satisfaction: 35 (score 4 or 5)
Lowentritt et al [74]	84	BNSRP (37) UNSRP (19) NNSRP (10)	IIEF-4	42
Marks et al [75]	14	NSRP (5) NNSRP (9)	IIEF-3 and IIEF-4	NSRP: 40 NNSRP: 0
Blander et al [76]	72	Unknown	IIEF-3 and IIEF-4	31
Feng et al [77]	53	BNSRP (21) UNSRP (15) NNSRP (17)	Erection sufficient for intercourse (single question)	BNSRP: 71 UNSRP: 80 NNSRP: 6
McMahon et al [82]	13	Not specified	IIEF-4	31 (score 4 or 5)
Zagaja et al [79]	170	BNSRP (59) UNSRP (41) NNSRP (20)	Erection adequate for intercourse in >50% of attempts	BNSRP: 53 UNSRP: 10 NNSRP: 0
Zippe et al [78]	91	BNSRP (53) UNSRP (12) NNSRP (26)	Ability for sexual intercourse (CCPP questionnaire)	BNSRP: 72 UNSRP: 50 NNSRP: 15
Baniel et al [83]	69	Not specified	Erection sufficient for vaginal intercourse	20
Martinez-Jabaloyas et al [84]	17	NNSRP (17)	SHIM	6
Ogura et al [85]	43	BNSRP (18) UNSRP (21) NNSRP (4)	IIEF-4 (n = 33)	BNSRP: 62 UNSRP: 54 NNSRP: 0
Raina et al [81]	174	BNSRP (104) UNSRP (28) NNSRP (42)	SHIM	BNSRP: 76 UNSRP: 53 NNSRP: 14
Shimizu et al [86]	13	BNSRP (8) UNSRP (5)	Erection sufficient for penetration	BNSRP: 100 UNSRP: 40

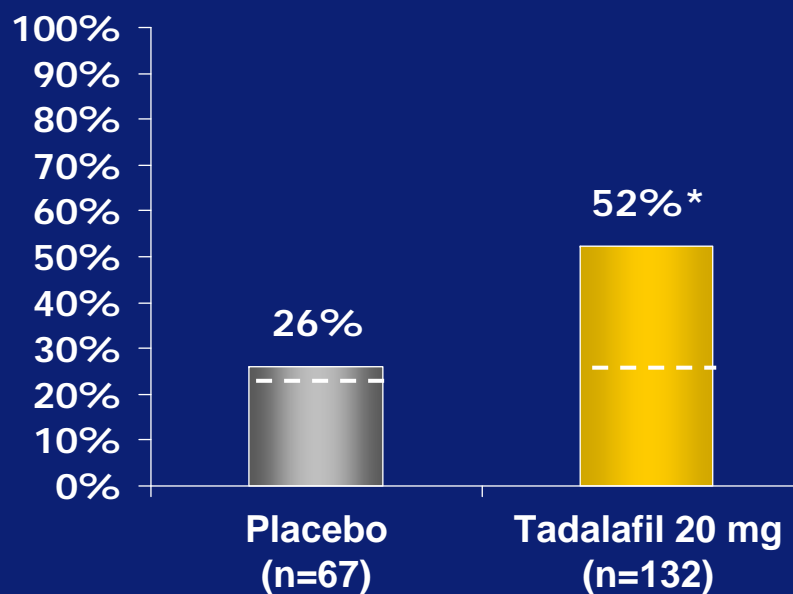
N = total number of post-RP ED patients treated with sildenafil; BNSRP = bilateral nerve-sparing radical prostatectomy; UNSRP = unilateral nerve-sparing radical prostatectomy; NNSRP = Non-nerve-sparing radical prostatectomy; NSRP = nerve-sparing radical prostatectomy; EDITS = Erectile Dysfunction Inventory of Treatment Satisfaction; IIEF = International Index of Erectile Function; IIEF-4 = IIEF question 4; IIEF-5 = IIEF question 5; SHIM = Sexual Health Inventory for Men (IIEF-5); CCPP = Cleveland Clinic Post Prostatectomy questionnaire.

Nerve-Sparing RP and Tadalafil

All Randomized Patients



Patients With Post-Operative Tumescence



* $P < 0.001$ vs. placebo
Montorsi et al., J Urol. 2004

Can ED be prevented in patients treated for PCa?



Recovery of erectile function after nerve-sparing radical prostatectomy: improvement with nightly low-dose sildenafil

Andreas Bannowsky*†, Heiko Schulze*,
Christof van der Horst*, Stefan Hautmann*,
Klaus-Peter Jünemann*

2008 BJU INTERNATIONAL | 101, 1279-1283 |

- N=23 vs 18 (no placebo)
- Rigiscan, IIEF
- Normal EF in 47% with sildenafil 25 mg vs 28%

FIG. 1. The recovery of EF after NSRP (41 men).

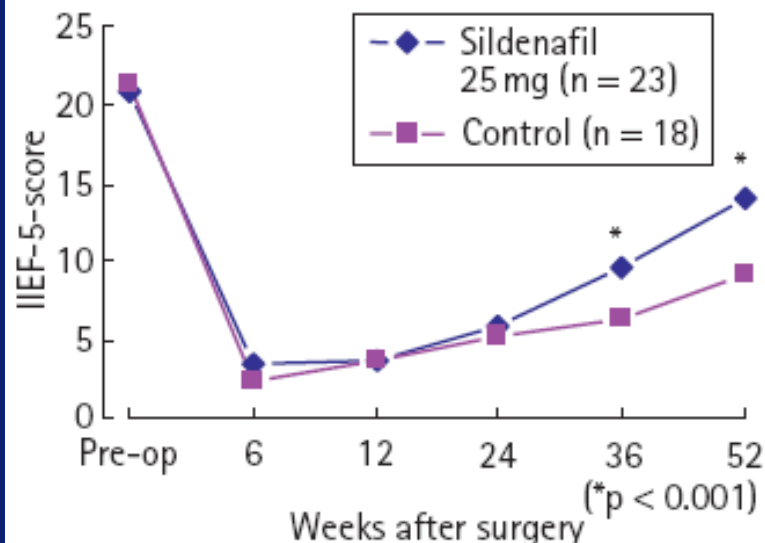
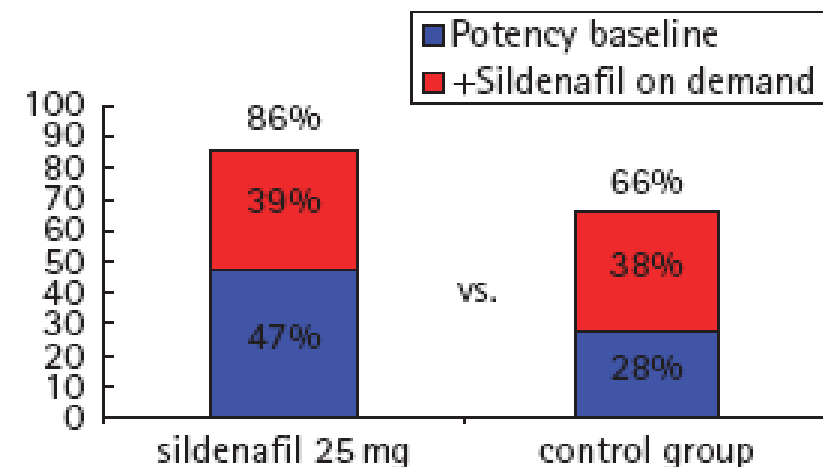


FIG. 2. Potency rate with and without low-dose sildenafil (25 mg) after NSRP.



Rationale: Clinical studies

Return of Nocturnal Erections and Erectile Function after Bilateral Nerve-sparing Radical Prostatectomy in Men Treated Nightly with Sildenafil Citrate: Subanalysis of a Longitudinal Randomized Double-blind Placebo-controlled Trial

Andrew R. McCullough, MD,* Laurence A. Levine, MD,[†] and Harin Padma-Nathan, MD[‡]

J Sex Med 2008;5:476–484.

- N=54, randomized trial after bilateral nerve-sparing RP
- Nightly sildenafil 50 mg, 100 mg or placebo 9 mos post-op
- Final assessment 8 weeks later, with no treatment
- **Normal EF in 24% with 50 mg, 33% with 100 mg and 5% with placebo**

Chronic Treatment with Tadalafil Improves Endothelial Function in Men with Increased Cardiovascular Risk

Giuseppe M.C. Rosano^{a,1}, Antonio Aversa^{b,1,*}, Cristiana Vitale^a, Andrea Fabbri^c, Massimo Fini^a, Giovanni Spera^b

^aCardiovascular Research Unit, Department of Medical Sciences, San Raffaele – Roma, TOSINVEST SANITA', Rome, Italy

^bDepartment of Medical Pathophysiology, University of Rome 'La Sapienza', Viale Policlinico 155, 00161 Rome, Italy

^cDepartment of Internal Medicine, University 'Tor Vergata', Endocrinology Unit, AfaR-CRCCS, Ospedale Fatebenefratelli Isola Tiberina, Rome, Italy

- N=32
- Tadalafil 20 mg, every other day or placebo
- Assessment at 4 weeks
- Brachial artery flow-mediated dilation and plasma levels of endothelin

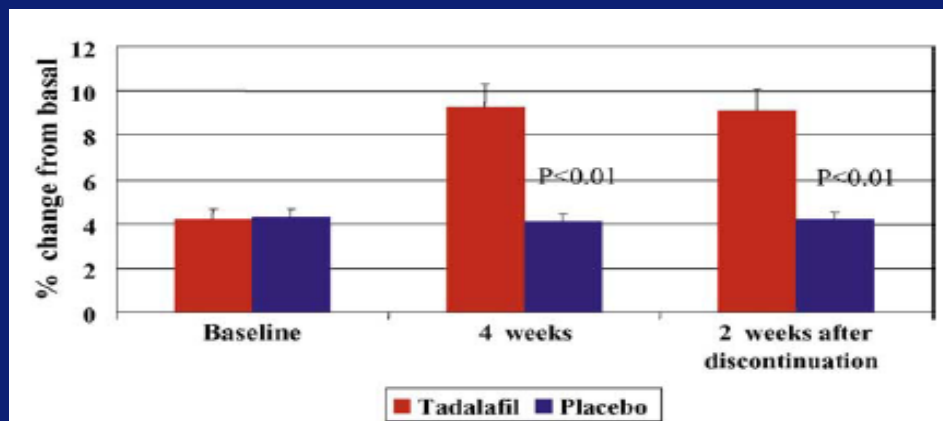


Fig. 1. Percent change compared to baseline in endothelial function (FMD) in patients treated with tadalafil and placebo after 4 weeks of therapy with Tadalafil 20 mg on alternate days and after 2 weeks of discontinuation of therapy. *p* values refer to comparison between tadalafil vs. placebo.

PDE5-i and Penile Rehabilitation

Controversy: Pros

- Hypoxia or absence of cavernosal oxygenation induces fibrosis of smooth muscles
- Fibrosis causes veno-occlusive dysfunction
Wayman et al., ESSM 2005, abstract
- Endothelial damage associated with vascular factors (metabolic syndrome)
- Trials with PDE5-i clearly show protection in diabetes and pts with high vascular risk factors, thus preventing cavernosal injury

Mulhall & Morgentaler, J Sex Med 2007

PDE5-i and Penile Rehabilitation

Controversy: Cons

- Very small studies
- Often no placebo arm, or no randomisation
- Short follow-up
- Need of standardized surgery procedures and assessment tools

Hatzimouratidis et al., Eur Urol 2009

Mulhall & Morgentaler, J Sex Med 2007

- On demand PDE5-i are effective

Briganti & Montorsi, Nat Clin Pract Urol 2006



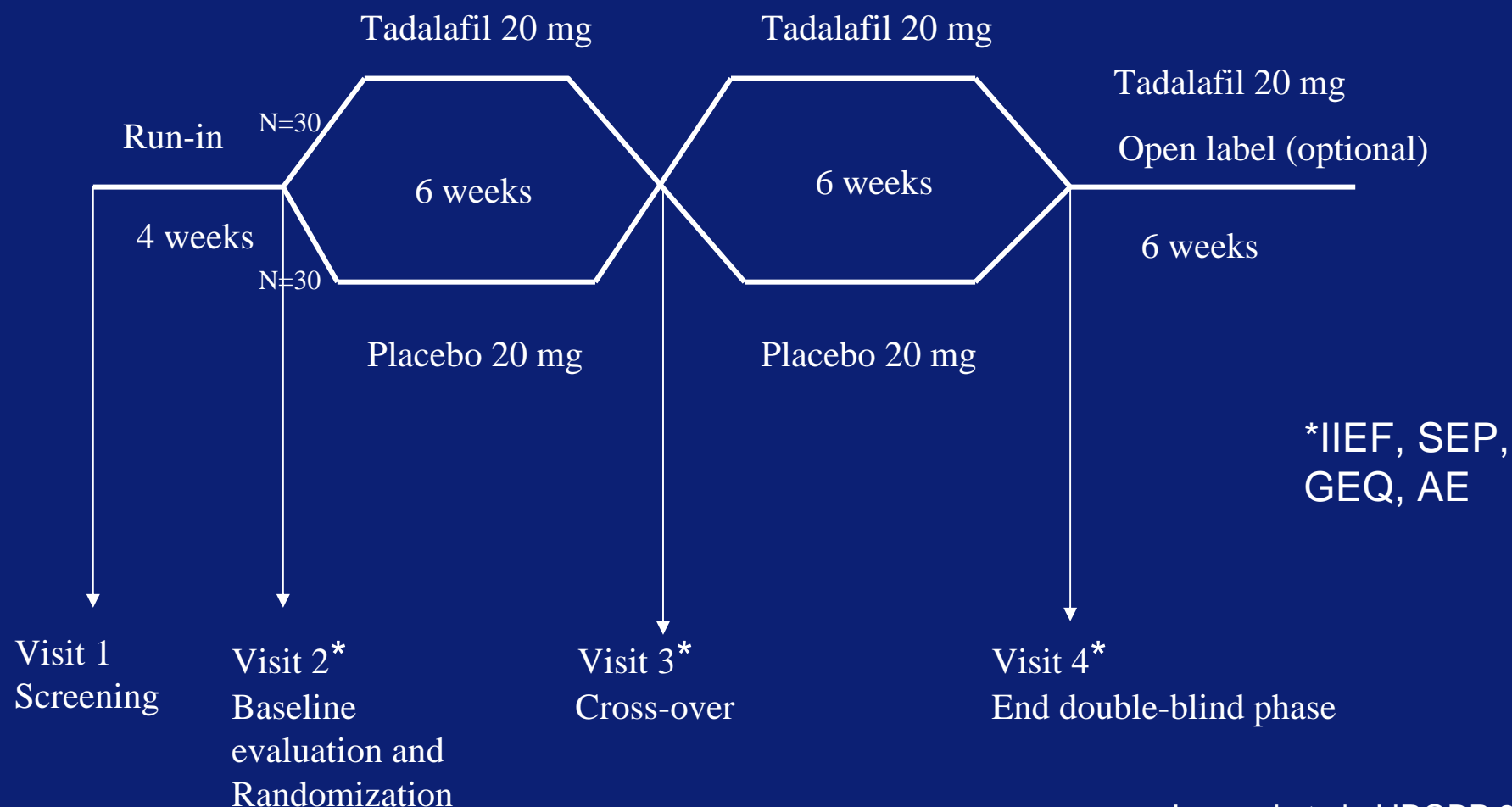
Radiotherapy

Tadalafil and ED after EBRT for PCa

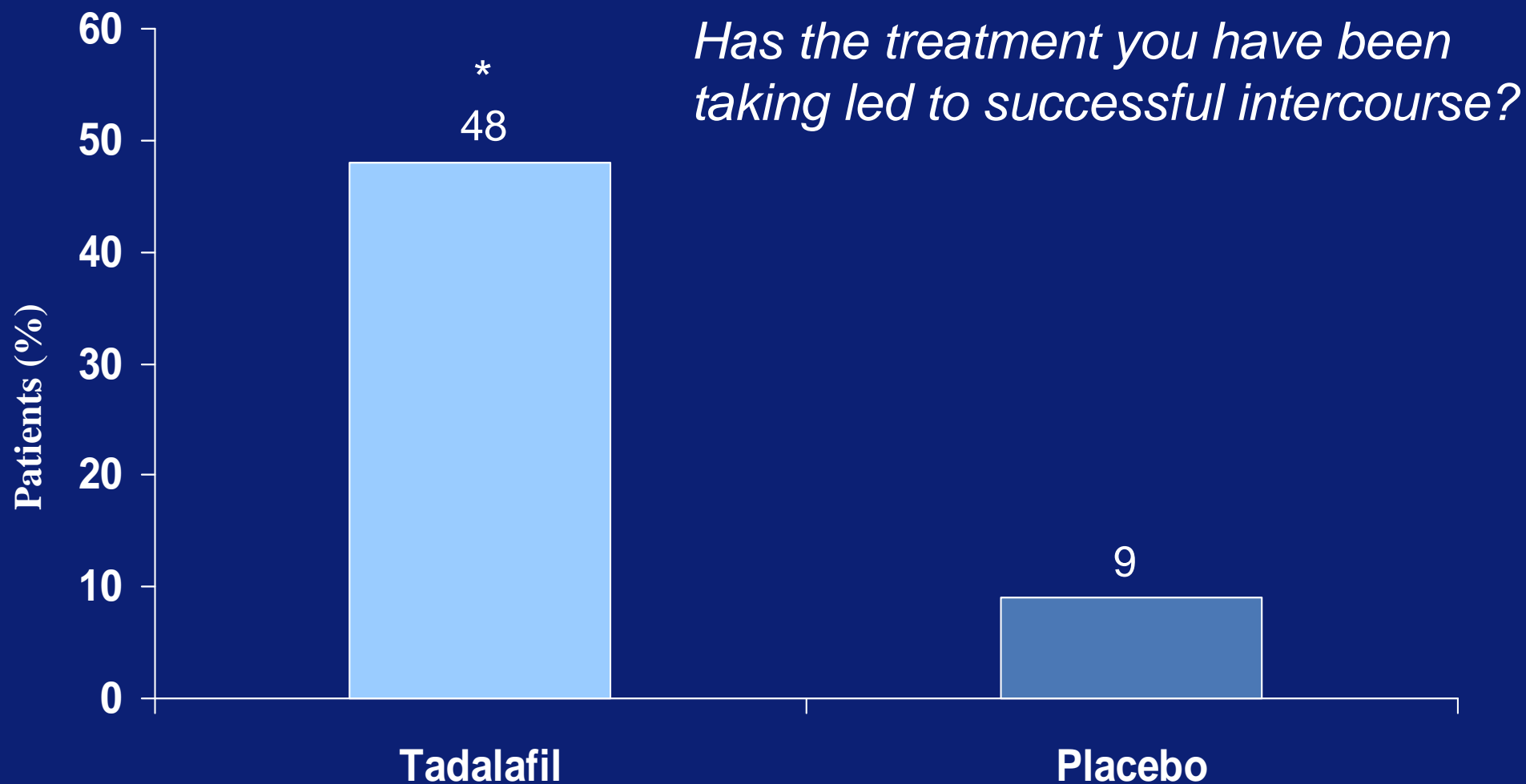
Study design

mean age 69 yrs

range 53-84 yrs



Tadalafil and ED after EBRT for PCa Results

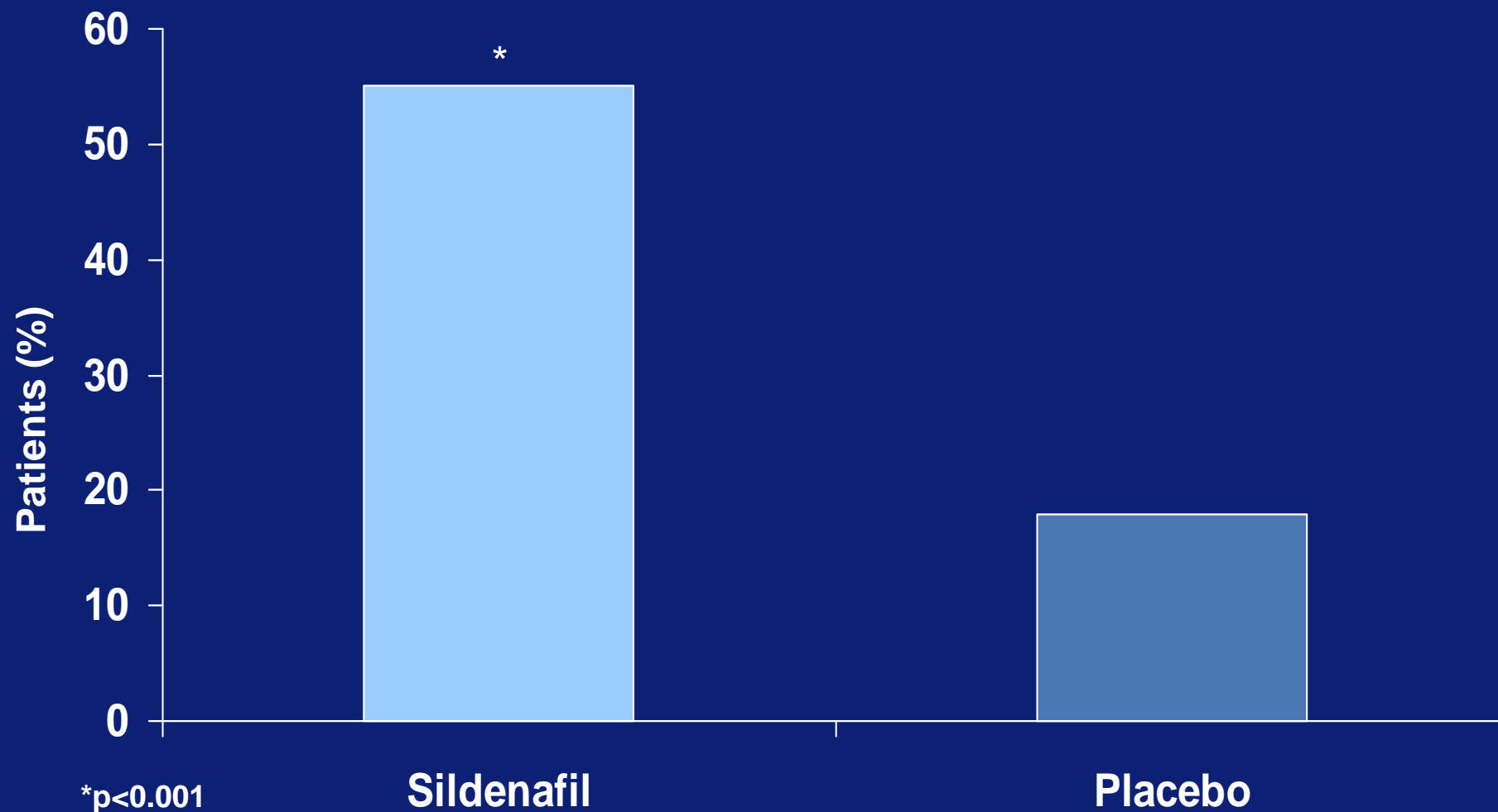


*p<0.001

Incrocci et al., IJROBP 2006

Sildenafil and ED after EBRT for PCa

Successful intercourse attempts

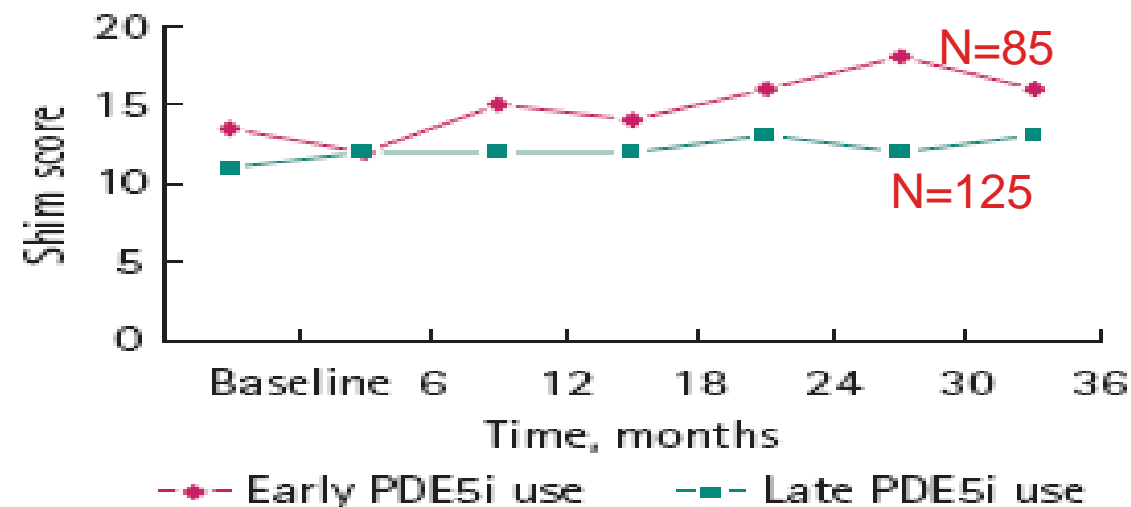


Early use of a phosphodiesterase inhibitor after brachytherapy restores and preserves erectile function

Jonathan D. Schiff, Natan Bar-Chama, Jaime Cesaretti and Richard Stock

- Sildenafil, vardenafil
- Mean age 62-63 yrs
- Retrospective

FIG. 1. Differences in SHIM scores at 18, 24, 30 and 36 months were significant, with $P = 0.04, 0.03, 0.04$ and 0.03 , respectively.



Couples

- Anxiety, depression, anger, financial difficulties and occupational changes may all contribute to the disruption of sexual activity
- Sexual activity dropped from 2 times weekly to once monthly during treatment in one study (Schover et al., 1987)
- Sexual problems developing after cancer treatment are caused by the emotional and medical impact of the disease and by the stress in the couple's relationship (Schover et al., 1987)

Couples (cont'd)

- Partner: Confrontation with chronic disease, avoid intimacy not to get sexually aroused, not to damage the male
- Need of time, patience and respect from the partner
- New erotic regions: inguinal regions, perineum, ears...

- On anatomy and location of treated organs
- On side effects and complications of surgery-radiotherapy-chemotherapy, including sexuality
- On sexual activities other than penetration
- The field of medicine needs to invest in the development of subspecialties such as oncosexology and rehabilitation sexology
- In a review of almost 400 patients, 73% needed to be seen only once or twice (Schover et al., 1998)

PDE5-i and Penile Rehabilitation Conclusion

- PDE5-i are effective to treat ED
- (Some) evidence that PDE5-i are effective in the rehabilitation process after surgery (no level 1 evidence-based literature)

Hatzimouratidis et al., Eur Urol 2009

- Need of randomized, prospective and well-powered trials

Cancer Survivorship and Sexual Health Symposium



June 17 – 19, 2011

Hyatt Regency Washington on Capitol Hill, Washington D.C. – USA



Over the last decade there have been significant improvements in the quality of health care men and women receive for sexual dysfunctions. The ISSM and SMSNA have adopted this image "The Challenge" for our conference as it symbolizes barriers and obstacles which must be overcome to address sexual health in cancer survivors.

Meeting Chairs

Gregory A. Broderick, USA
Luca Incrocci, The Netherlands

Advisory Board

Edgardo Becher, Argentina
Arthur L. Burnett, USA
John Dean, United Kingdom
Craig F. Donatucci, USA
Annamaria Giralaldi, Denmark
Wayne Hellstrom, USA
John P. Mulhall, USA
Ajay Nehra, USA
Ira Sharlip, USA
Ronald W. Lewis, USA

Lilly Oncology On Canvas, an art exhibition honoring the physical and emotional journeys people face when confronted by a cancer diagnosis, will be on display at this meeting. The image shown above is a photograph submitted by a healthcare professional to LOOC, 2008.



www.cancersurvivorsandsex.org

Erasmus MC



Thanks

See you all in Washington!