Answers That Matter.

Breakfast Session

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Urologist
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Who Benefits Most from Daily Tadalafil - Eli Lilly Breakfast Session

Saturday, 22 June 2013 Start 7:00am Duration: 60mins Baytrust

CIALIS® (tadalafil) for ED* and LUTS/BPH^

Tony Nixon

June 2013

***Erectile dysfunction**
^Lower urinary tract symptoms associated with benign prostatic hyperplasia

Disclosure

- I declare that I have received an honorarium from Lilly for this presentation.
- I have no other disclosures to declare.

Overview

- Erectile dysfunction (ED) in the context of general male health and well-being
- Psychosocial impact of ED
- Pharmacological management of ED – once-a-day (OAD) dosing
- Potential links between ED and LUTS
- Pharmacological management of LUTS – PDE5 inhibitor tadalafil as a OAD therapeutic option

CIALIS® (tadalafil) for ED and LUTS/BPH

Erectile dysfunction (ED) in the context of general male health and well-being

ED in Australia and New Zealand

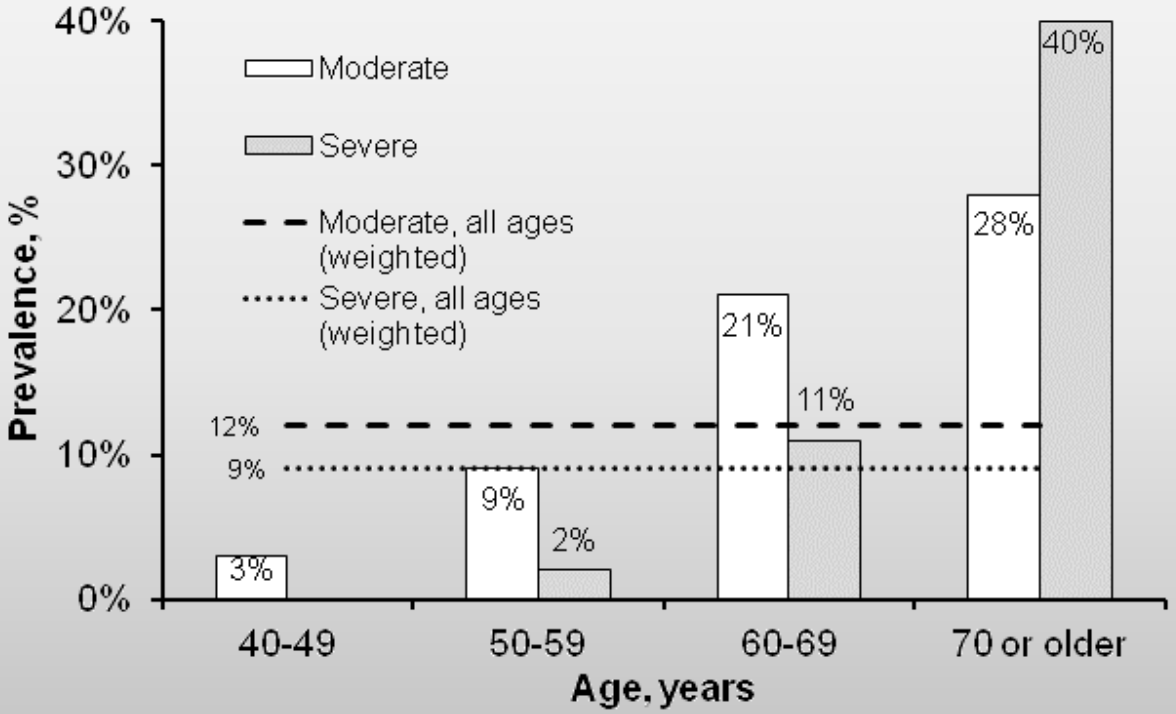
- ED is an inability to achieve an erection that allows sexual activity with penetration[1]
- Erection problems can be psychogenic or organic in origin, or due to mixed factors[2]
- ED is common and prevalence increases with age[3]

References

1. NIH Consensus Development Panel on Impotence. *JAMA* 1993; 270: 83–90.
2. Clinical summary guide. Erectile dysfunction: diagnosis and management. Clayton, Vic: Andrology Australia, 2010. www.andrologyaustralia.org/health-professionals/clinical-summary-guidelines/. Accessed February 2013.
3. Holden CA et al. *Lancet* 2005; 366: 218–24.

ED is more common and more severe as men age[1]

ED prevalence by severity, men aged ≥ 40 years in Australia[1]

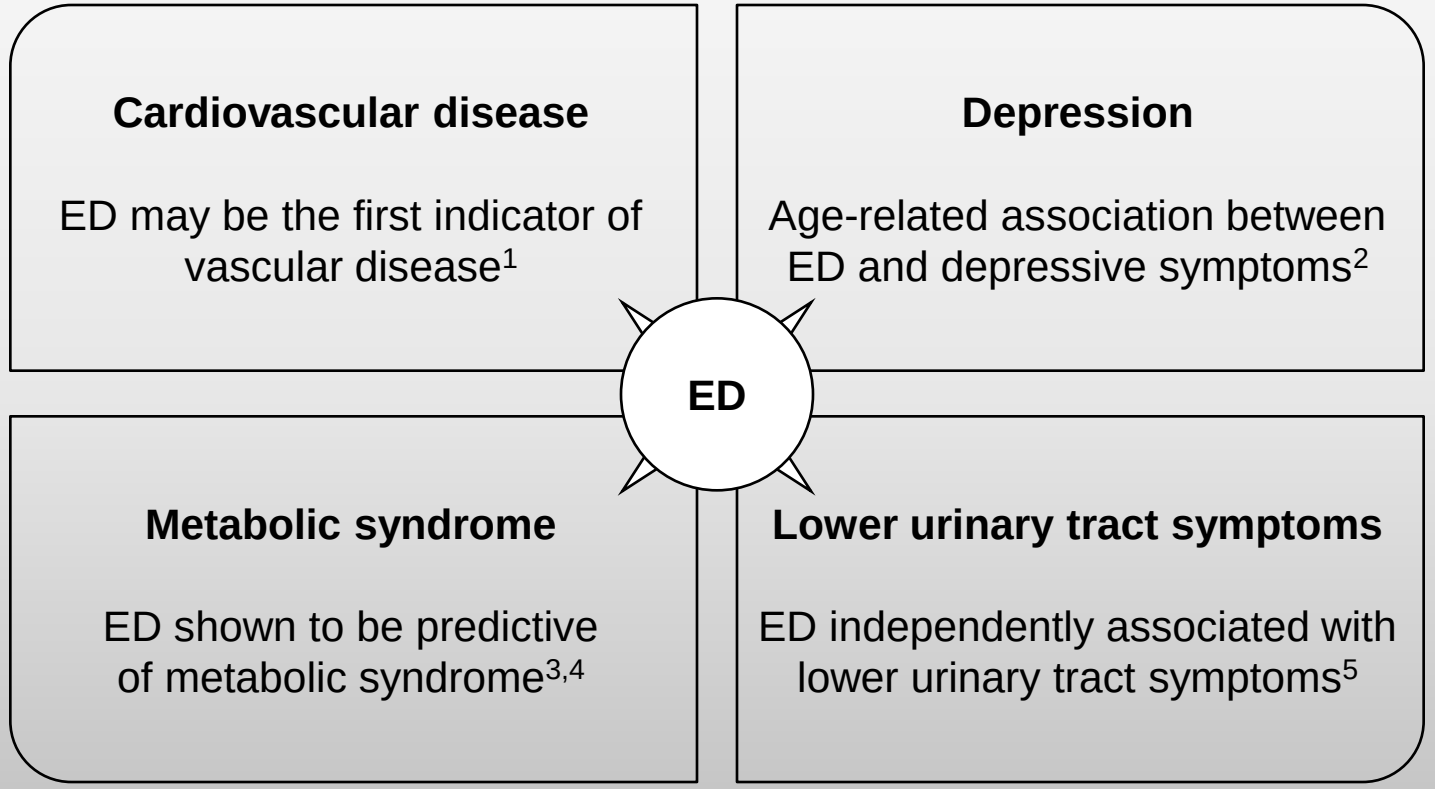


Adapted from Holden et al. 2005.[1]

Reference

1. Holden CA et al. *Lancet* 2005; 366: 218–24.

ED is associated with a number of other conditions



References

1. Benard F. *Can Urol Assoc J* 2011; 5: 352–3.
2. Araujo AB et al. *Psychosom Med* 1998; 60: 458–65.
3. Kupelian V et al. *J Urol* 2006; 176: 222–6.
4. Esposito K et al. *Diabetes Care* 2005; 28: 1201–3.
5. Rhoden EL et al. *J Sex Med* 2008; 5: 2662–8.

CIALIS® (tadalafil) for ED and LUTS/BPH

Psychosocial impact of ED

Not just about sex: the broad psychosocial impact of ED

- ED is a condition that can affect more than male erectile functioning[1]

- ED has an impact on patient sexual quality of life and other psychosocial outcomes[1,2]
  - Lack of response impacts daily life[3]
  - Erection problems extend beyond sexual intercourse and are present around the clock[3]
  - Treating erection problems also involves non-physical dimensions[3]

References

1. Althof SE. *Urology* 2002; 59: 803–10.
2. Althof SE. *Int J Impot Res* 2002; 14 (Suppl 1): S99–104.
3. Galaxy Research. Erection problems: Voice of the Patient survey, 2011. Prepared for Eli Lilly Australia.

Voice of Australian Men: survey[1]

- The survey sought to quantify the:
  - Extent to which erection problems extend beyond sex
  - Impact of erection problems beyond sex
  - Importance of addressing erection problems beyond sex

- 1010 men (aged 40–69 years) with ED completed the survey
  - Most sufferers (81%) consider ED to be a problem for them, including 31% who consider it a major problem
  - 70% of those with mild symptoms admit their erection difficulties are a problem for them
    - This figure rises to 90% or more for those with moderate or severe symptoms

Reference

1. Galaxy Research. Erection problems: Voice of the Patient survey, 2011. Prepared for Eli Lilly Australia.

ED has a psychological impact[1]

- Anxiety
  - For approximately 43% of the surveyed men, just the thought of having sex can bring on anxiety
- Confidence
  - 59% of ED sufferers have experienced a lack of confidence when interacting with a person they find attractive because it reminds them of their ED
- Masculinity
  - Around half of ED sufferers consider an erection a sign of virility and without it would feel a loss of their manhood
  - 54% report they would feel less of a man if they couldn't get an erection

Reference

1. Galaxy Research. Erection problems: Voice of the Patient survey, 2011. Prepared for Eli Lilly Australia.

What is important to the patient and why do they seek treatment?

- Having a healthy sex life is important to most men (90%)[1]
- Getting an erection when desired is important for men and women[1,2]
- 60% indicate that treatment allows them to have sex, but only 35% cite this as the main reason they sought treatment[1]
- Other factors for seeking treatment are:[1]
  - To feel normal again (42%)
  - To feel like a man again (29%)
  - Because it is important in their day-to-day life (22%)

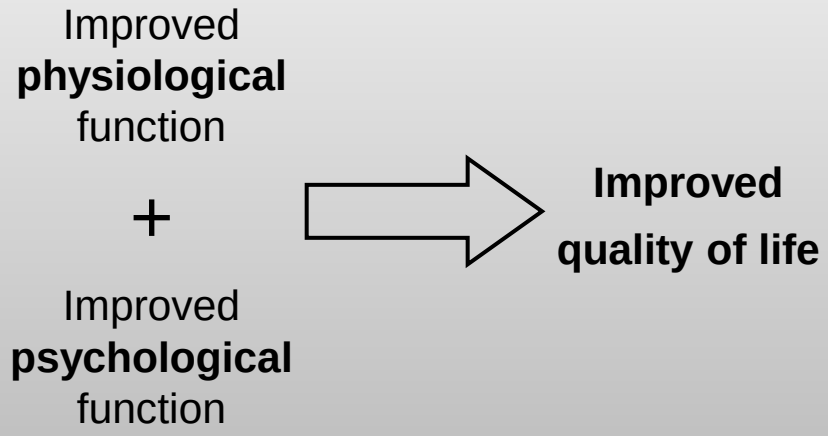
References

1. Galaxy Research. Erection problems: Voice of the Patient survey, 2011. Prepared for Eli Lilly Australia.
2. Mulhall J et al. *J Sex Med* 2008; 5: 788–95.

ED treatment: not just about sex

- Important to treat the whole man
  - Treating erection problems isn't simply about sex[1]
  - ED treatment may improve many aspects of a man's mental well-being,[2] quality of life[3] and a couple's relationship[4]

ED management

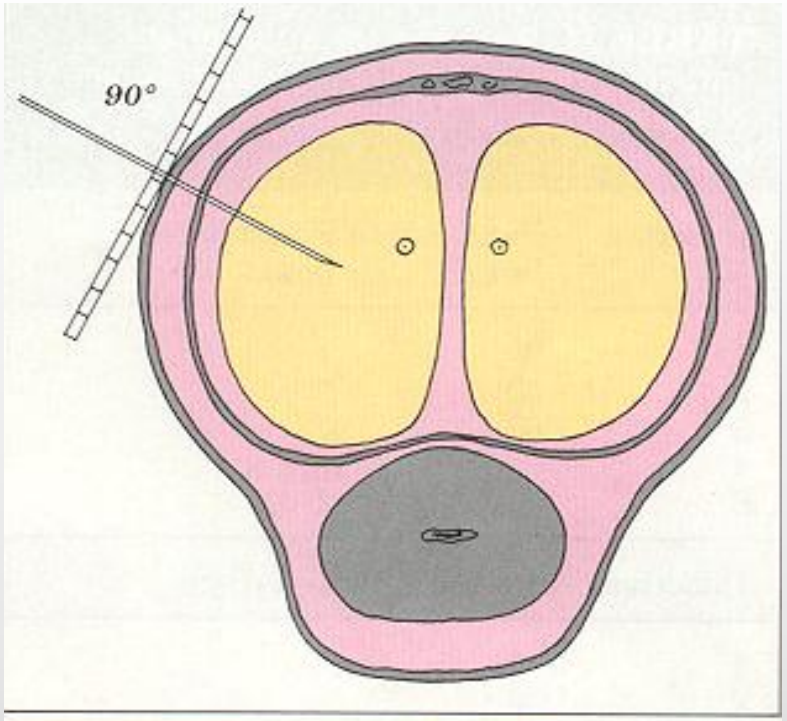


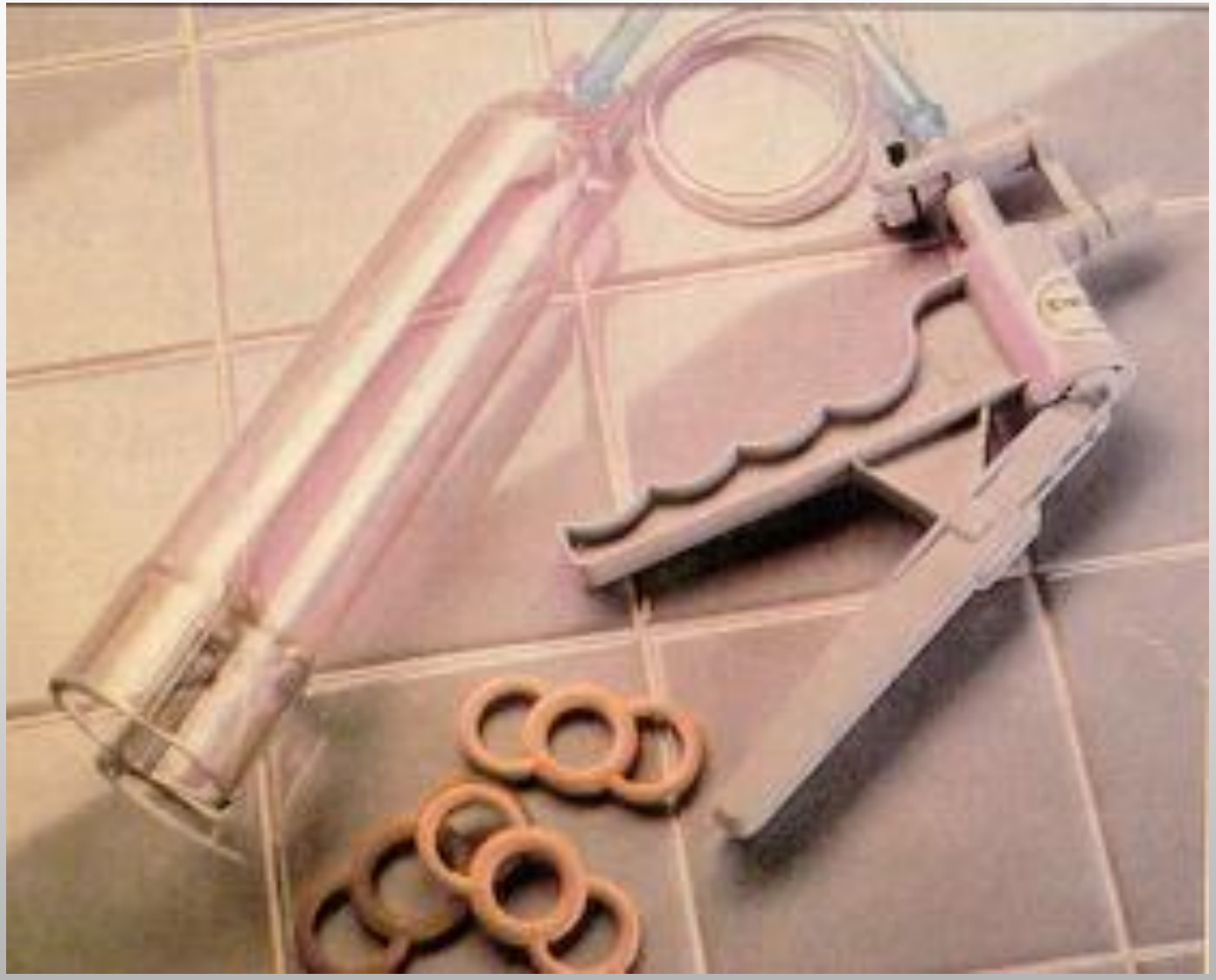
References

1. Hanson-Divers C et al. *J Urol* 1998; 159: 1541–7.
2. Costa P et al. *Int J Impot Res* 2003; 15: 173–84.
3. Latini D et al. *J Urol* 2003; 169: 1437–42.
4. Rubio-Aurioles E et al. *J Sex Med* 2009; 6: 1314–23.

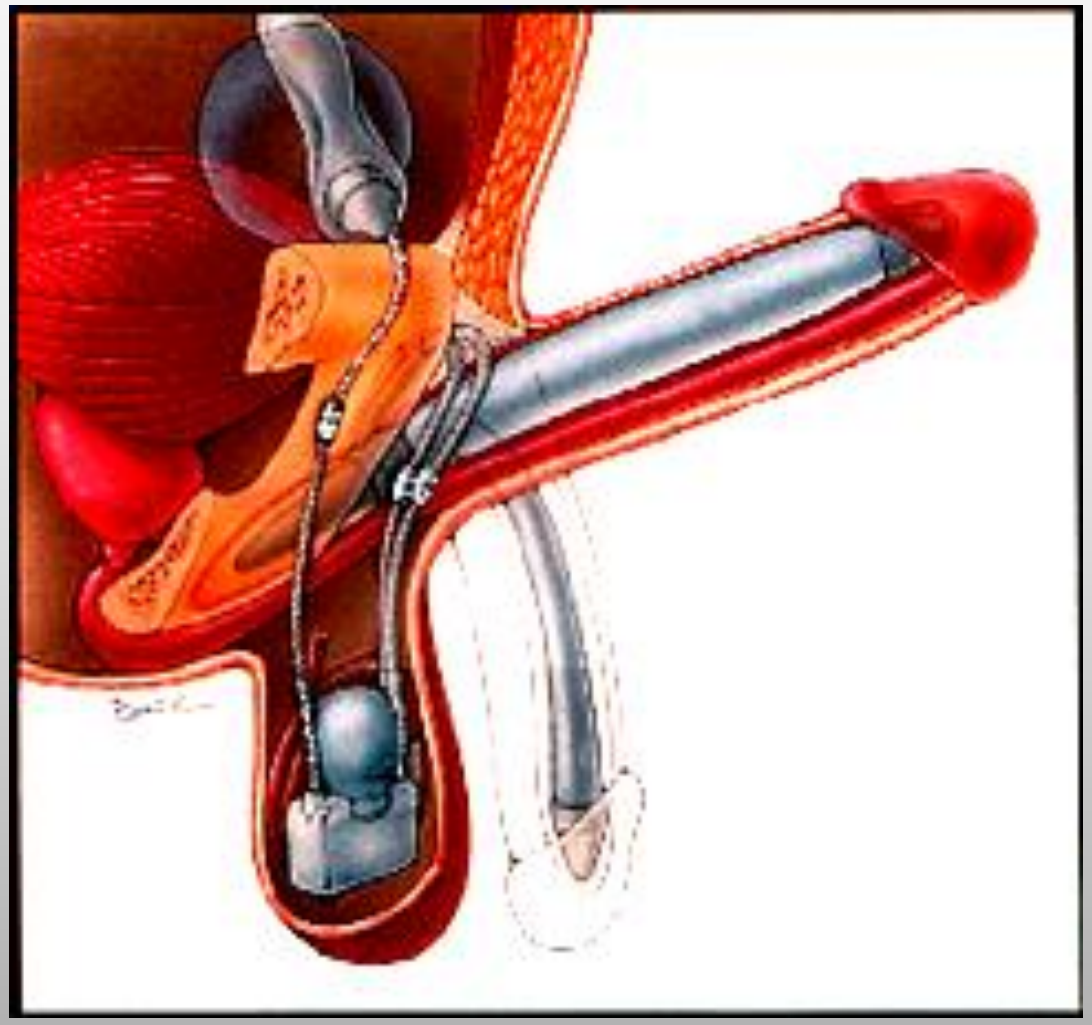
Treatment of ED

- Oral therapy
  - Tadalafil
  - Vardenafil
  - Sildenafil
- Injection therapy
- Vacuum pump devices
- Penile implants


90°



Inflatable prosthesis



CIALIS® (tadalafil) for ED and LUTS/BPH

Pharmacological management of ED – once-a-day dosing

Pharmacological differences of PDE5 inhibitors

PDE5 inhibitor	Time to maximum plasma concentration (t_{max}) (hours)	Elimination half-life ($t_{1/2}$) (hours)
Sildenafil[1]	1* (0.5–2.0)	3.0–5.0
Tadalafil[2]	2 (0.5–12.0)	17.5
Vardenafil[3]	1* (0.5–2.0)	4.0–5.0

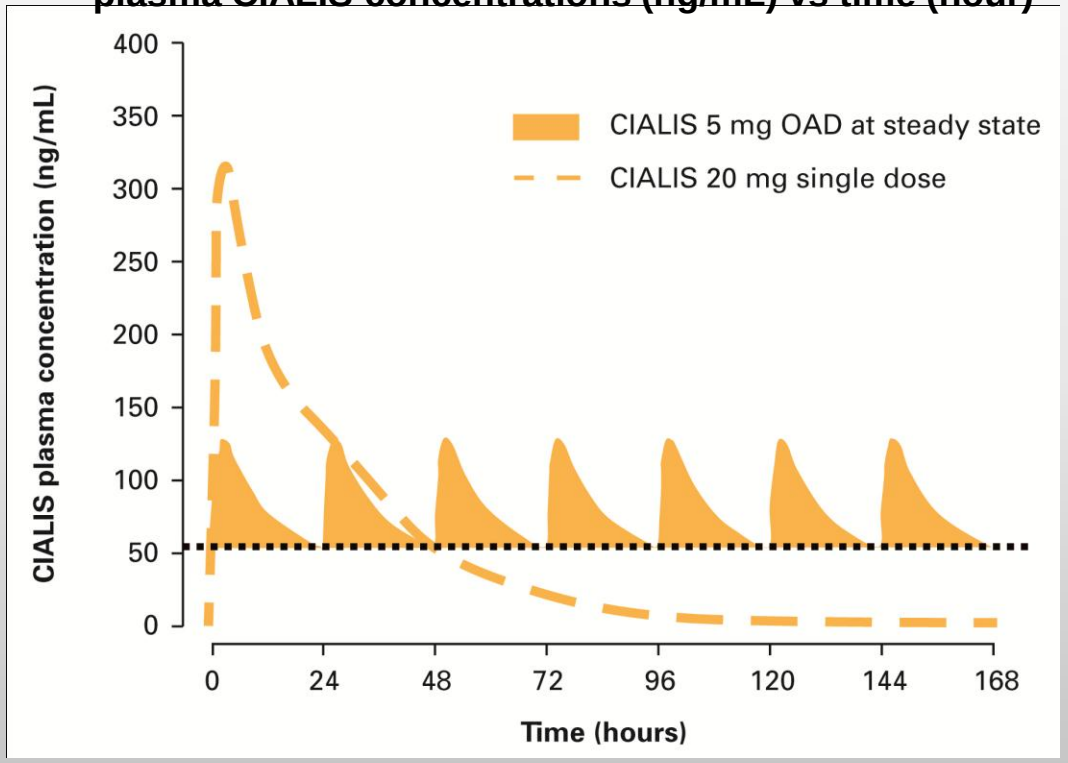
PDE5, phosphodiesterase type 5.
*Dependent on food intake (i.e. slower resorption of the drug and increase in t_{max} by approximately 1 hour after a fatty meal).

References

1. VIAGRA Data Sheet. Date of preparation: 22 January 2008.
2. CIALIS Data Sheet. Date of preparation: 31 January 2013.
3. LEVITRA Data Sheet. Date of preparation: 16 December 2011.

Predicted CIALIS 5 mg OAD concentration at steady state[1]

Predicted (5 mg OAD) and measured (20 mg single dose) plasma CIALIS concentrations (ng/mL) vs time (hour)



PDE5, phosphodiesterase type 5 inhibitor.
Adapted from Wrishko et al. 2009.[1]

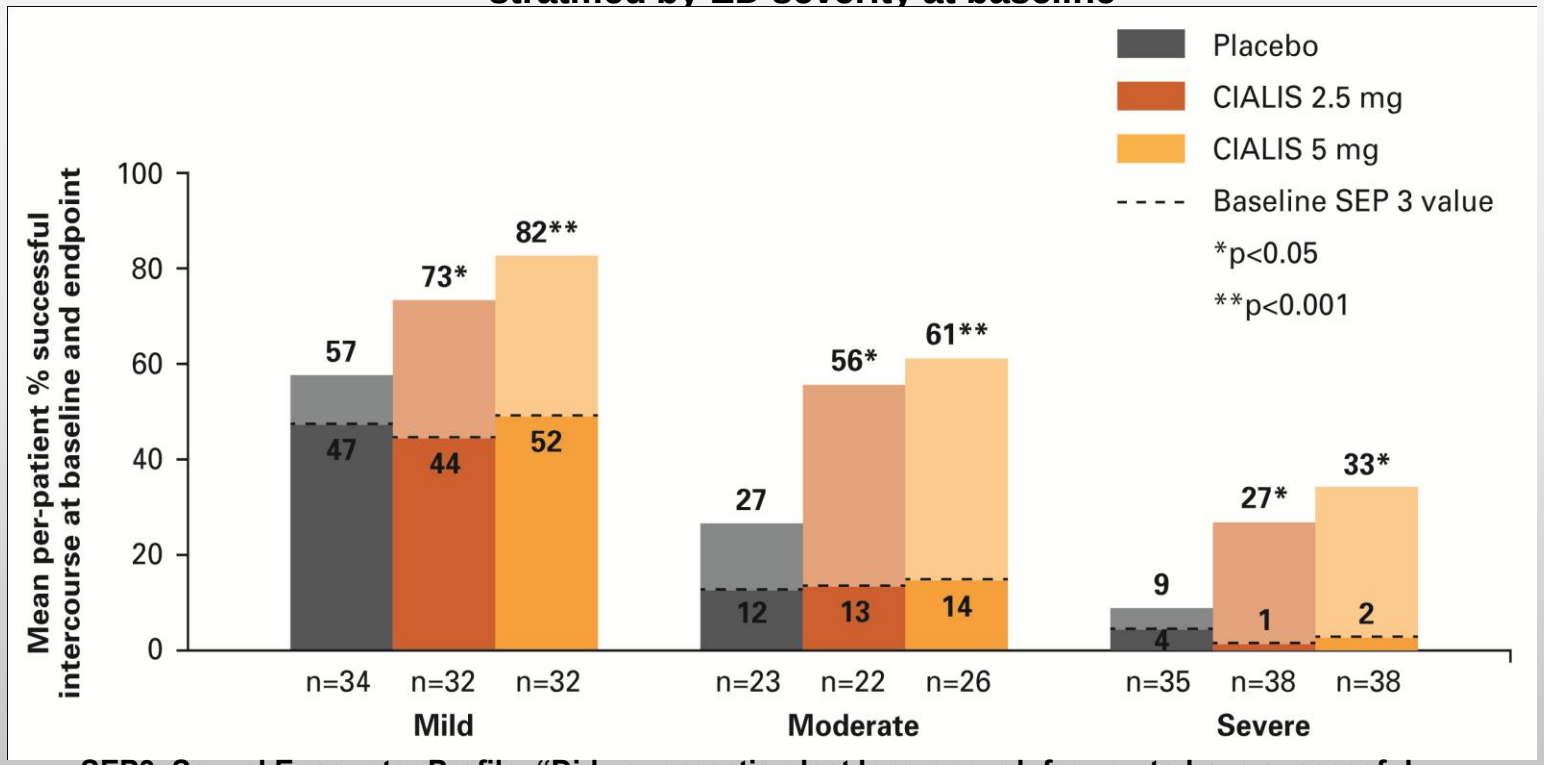
- A total plasma concentration of 55 ng/mL corresponds to 90% inhibition of PDE5
- A 5 mg daily dosing regimen at steady state provides a predicted plasma concentration above or near 55 ng/mL for almost the entire dosing interval

Reference

1. Wrishko R et al. *J Sex Med* 2009; 6: 2039–48.

Significant improvement in erectile function, maintained for 6 months[1]

Mean per-patient SEP3 score at 24-week endpoint for patients stratified by ED severity at baseline



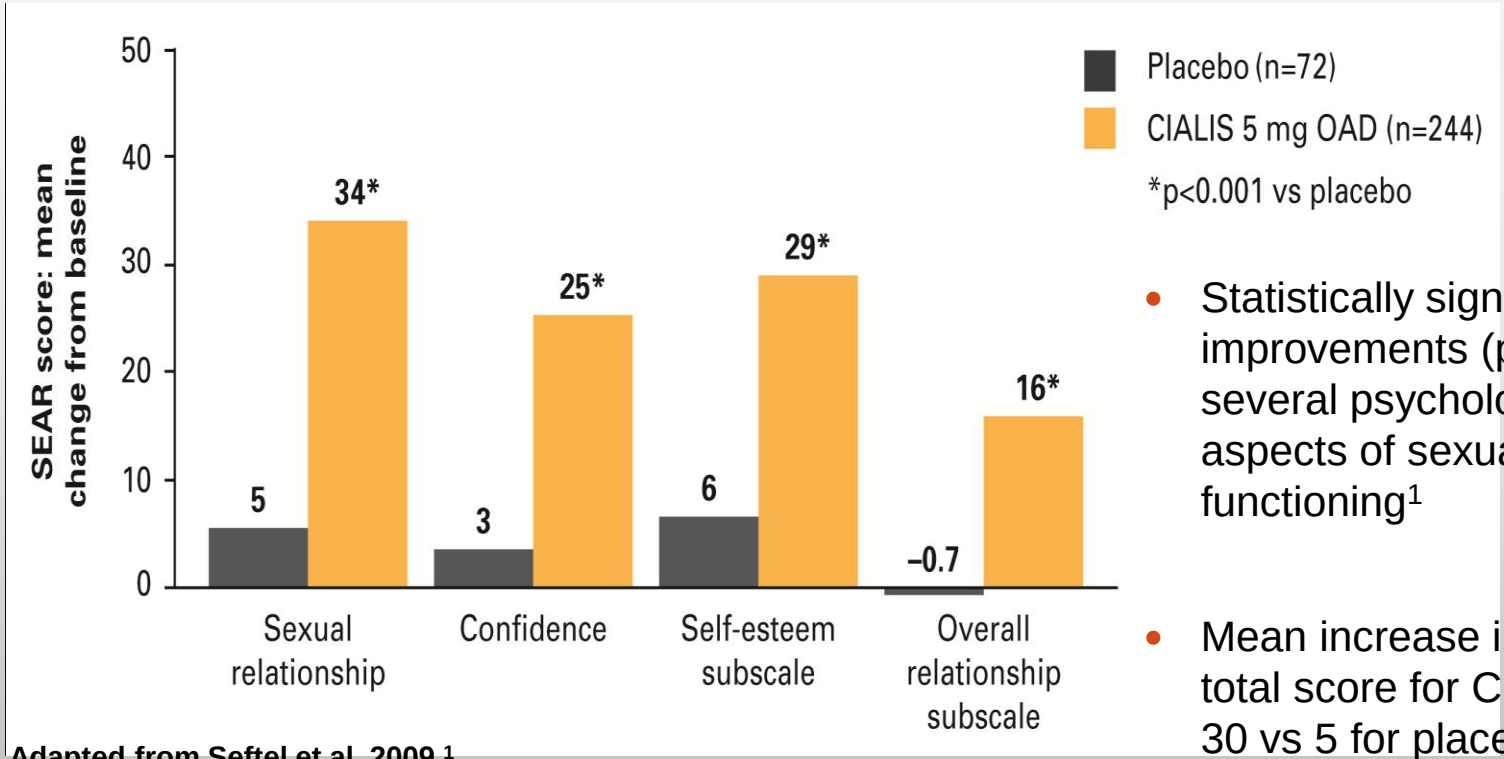
SEP3, Sexual Encounter Profile: "Did your erection last long enough for you to have successful intercourse?"
Adapted from Rajfer et al. 2007.[1]

Reference

1. Rajfer J et al. *Int J Impot Res* 2007; 19: 95–103.

Restores confidence and self-esteem[1]

Mean change from baseline in Self-Esteem And Relationship (SEAR) score



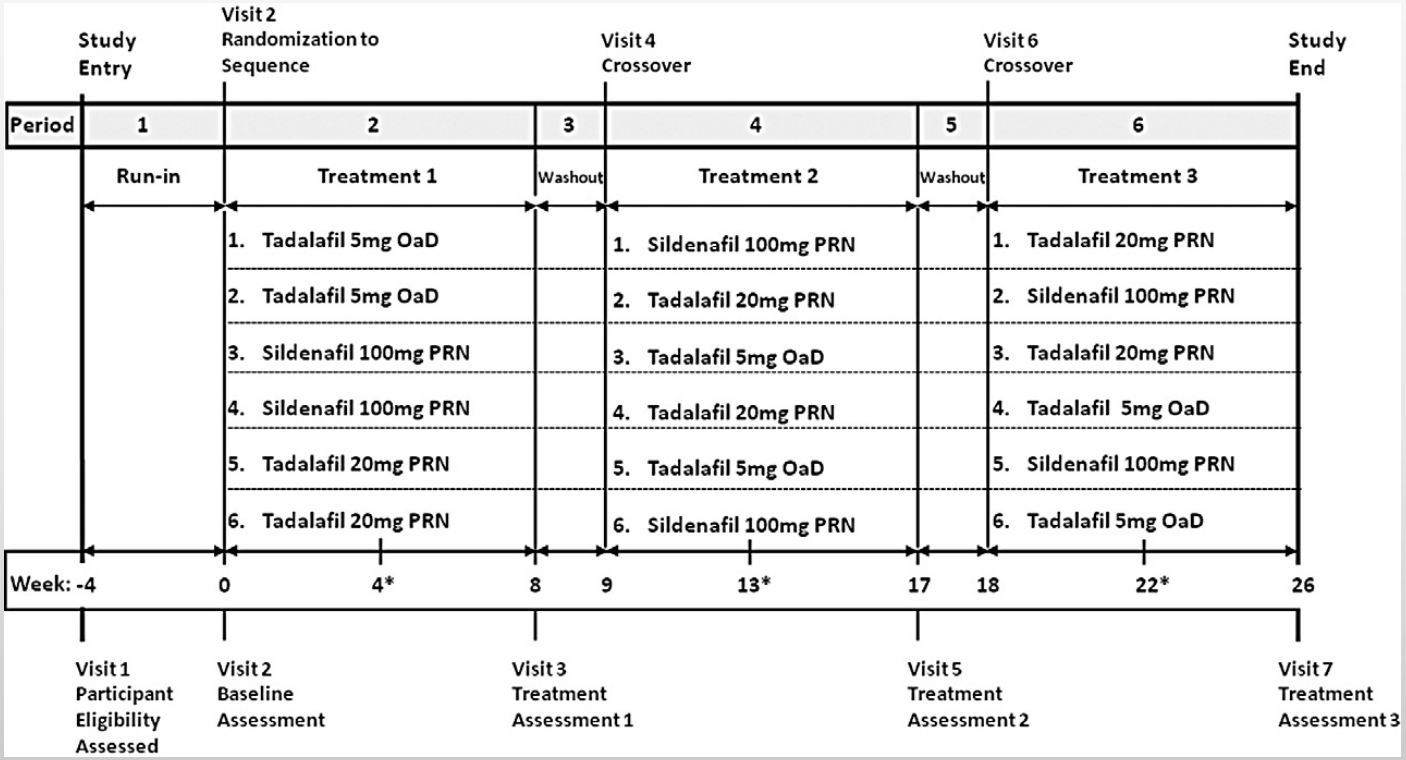
- Statistically significant improvements ($p<0.001$) in several psychological aspects of sexual functioning[1]
- Mean increase in SEAR total score for CIALIS was 30 vs 5 for placebo

Adapted from Seftel et al. 2009.[1]

Reference

1. Seftel AD et al. *Int J Impot Res* 2009; 21: 240–8.

OAD compared with on-demand therapy for ED[1]



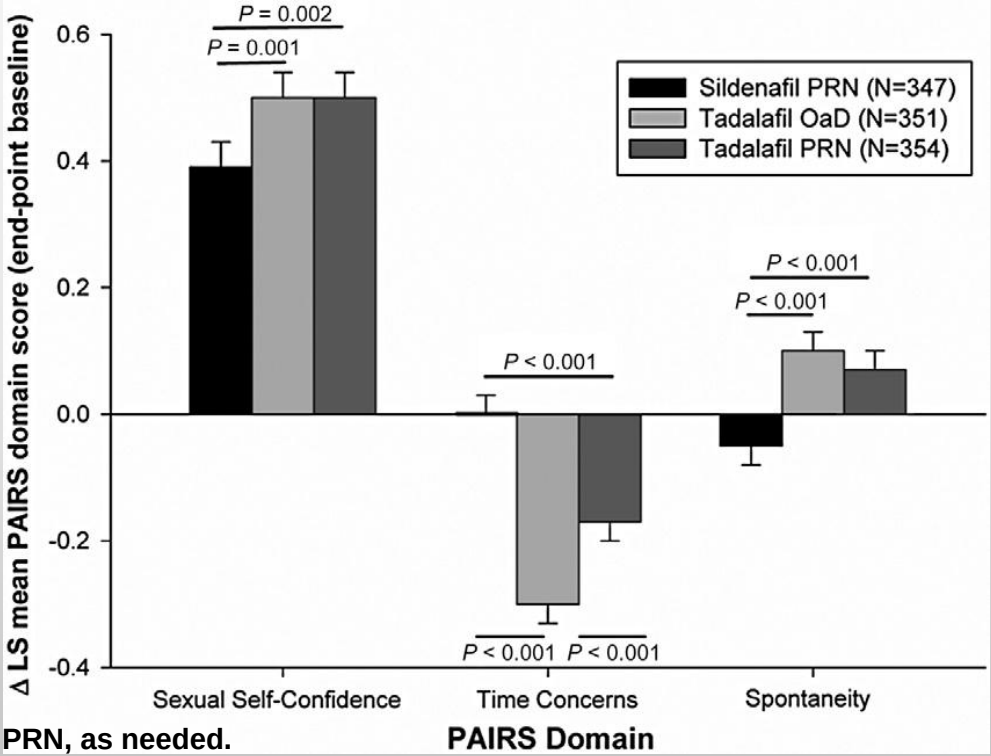
*Unscheduled visits for dose adjustment were permitted during the first 4 weeks of each treatment phase. Dose adjustments were not permitted during the final 4 weeks of each treatment phase.

Reference

1. Rubio-Aurioles E et al. *J Sex Med* 2012; 9: 1418–29.

OAD compared with on-demand therapy for ED[1]

Change in Psychological and Interpersonal Relationship Scales (PAIRS) domain score following PDE5 inhibitor treatment



PRN, as needed.

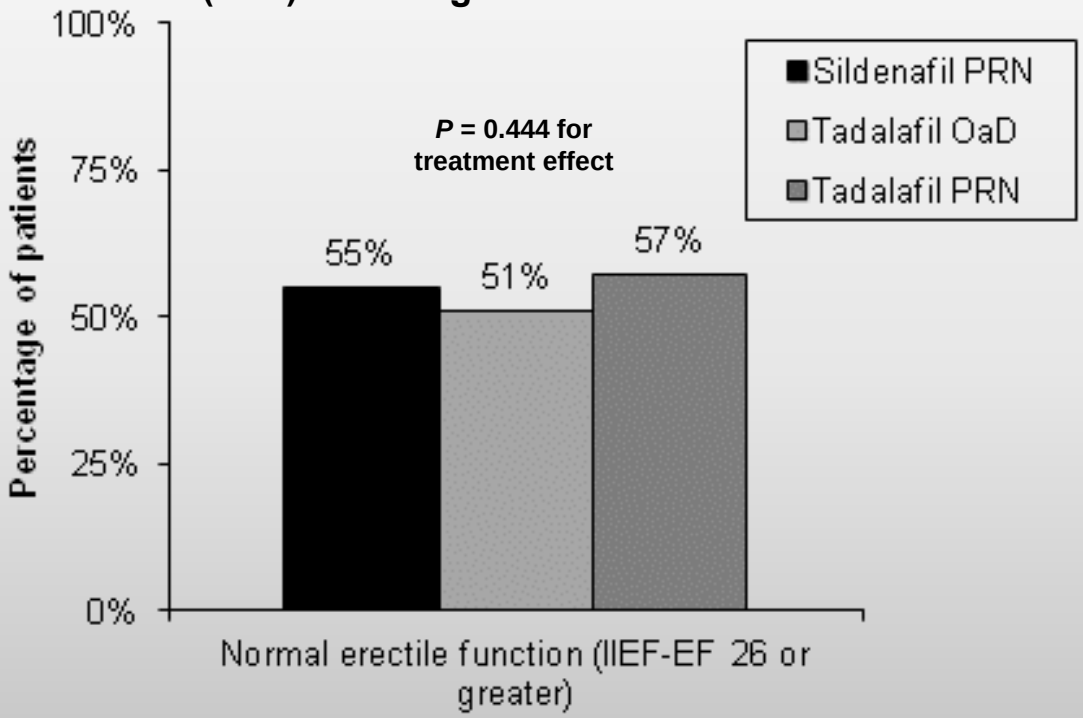
Adapted from Rubio-Aurioles et al. 2012.[1]

Reference

1. Rubio-Aurioles E et al. *J Sex Med* 2012; 9: 1418–29.

CIALIS 5 mg OAD improves erectile function[1]

Percentage of patients with normal IIEF-EF (≥ 26) following PDE5 inhibitor treatment



IIEF-EF, International Index of Erectile Function-Erectile Function domain; PDE5, phosphodiesterase type 5; PRN, as needed.
Adapted from Rubio-Aurioles et al. 2012.[1]

Reference

1. Rubio-Aurioles E et al. *J Sex Med* 2012; 9: 1418–29.

OAD and PRN pharmacotherapy for ED[1]

- First comparative trial between ‘once-a-day’ and ‘on-demand’ pharmacotherapy for ED
- Significantly greater improvement in sexual self-confidence with CIALIS OAD
- Significant reduction in time concerns with CIALIS OAD that can differentiate it from other PRN treatments
- Statistical significance in favour of CIALIS OAD was reported for time concerns and morning erection
  - Similar IIEF-EF outcomes for OAD therapy when compared to PDE5 inhibitors on-demand
- CIALIS OAD is well tolerated and the treatment-emergent adverse event (TEAE) profile is consistent with the literature

Reference

1. Rubio-Aurioles E et al. *J Sex Med* 2012; 9: 1418–29.

Safety and tolerability for CIALIS OAD for ED[1]

TEAEs reported by ≥ 2% of patients treated with CIALIS 2.5 mg or 5 mg OAD for ED and more frequent on drug than placebo in phase III studies

System organ class	Adverse event	CIALIS (n=647) %	Placebo (n=318) %
Gastrointestinal disorders	Dyspepsia	3.9	1.3
Infections and infestations	Nasopharyngitis	3.4	3.1
	Influenza	2.0	1.9
	Upper respiratory tract infection	2.2	0.9
Musculoskeletal and connective tissue disorders	Back pain	2.9	1.3
	Myalgia	2.3	0.9

Please review the full CIALIS Data Sheet for a complete list of contraindications, precautions and interactions

Reference

1. CIALIS Data Sheet. Date of preparation: 31 January 2013.

CIALIS 5 mg OAD is well tolerated[1–4]

- Most AEs reported have been considered by patients as mild or moderate; the most common include headache, nasal congestion and back pain[1]
- The discontinuation rate of CIALIS due to AEs is low[1]
- CIALIS is contraindicated in patients using nitrates and those with unstable cardiac disease, non-arterial ischaemic optic neuropathy (NAION) and hypersensitivity[1]
- Caution is advised when patients combine CIALIS with alpha-blockers[1]
- Please review full Product Information before prescribing

References

1. CIALIS Data Sheet. Date of preparation: 31 January 2013.
2. Rajfer J et al. *Int J Impot Res* 2007; 19: 95–103.
3. Seftel AD et al. *Int J Impot Res* 2009; 21: 240–8.
4. Rubio-Aurioles E et al. *J Sex Med* 2012; 9: 1418–29.

Key messages

- ED coexists with a number of other conditions
- It is important to recognise the psychosocial impact associated with ED
- When choosing a treatment, it is important to consider all aspects of ED
  - Comorbidities
  - Psychosocial impacts
- CIALIS OAD is well tolerated and has proven efficacy for ED
- CIALIS OAD can also address psychosocial factors
  - Significantly improves sexual relationship, confidence and self-esteem

References

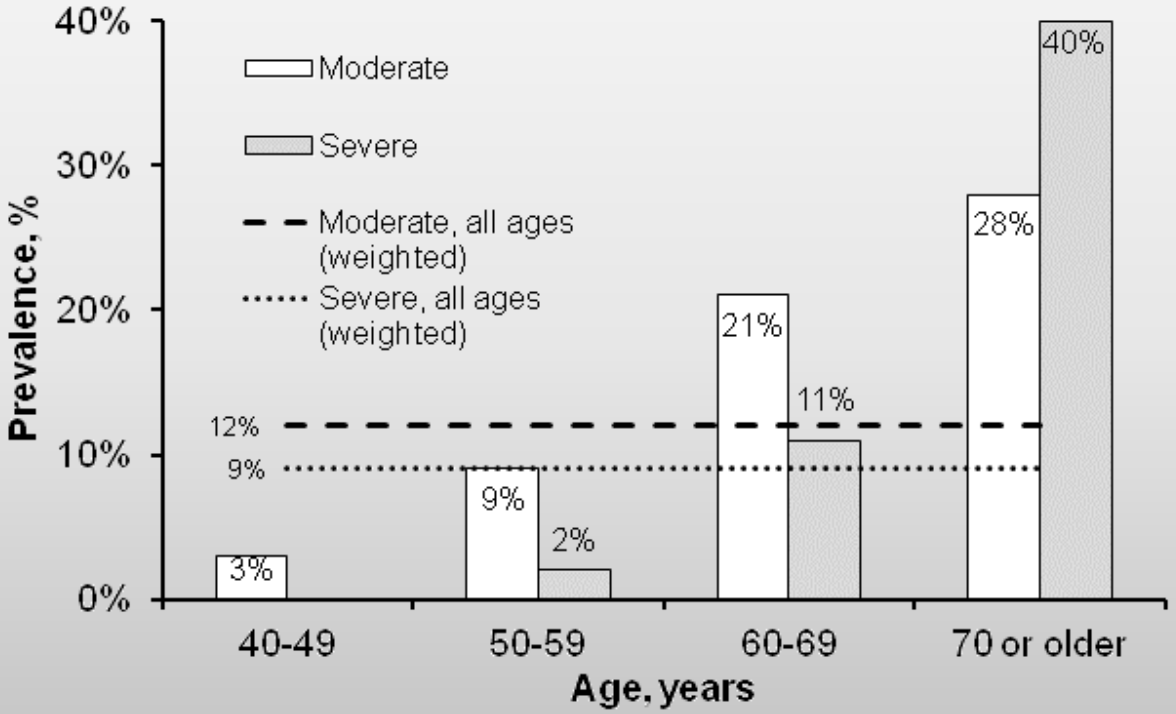
Please refer to the ‘Reference list’ on the last slide of this presentation.

CIALIS® (tadalafil) for ED and LUTS/BPH

Potential links between ED and LUTS

ED is more common and more severe as men age[1]

ED prevalence by severity, men aged ≥ 40 years in Australia[1]



Adapted from Holden et al. 2005.[1]

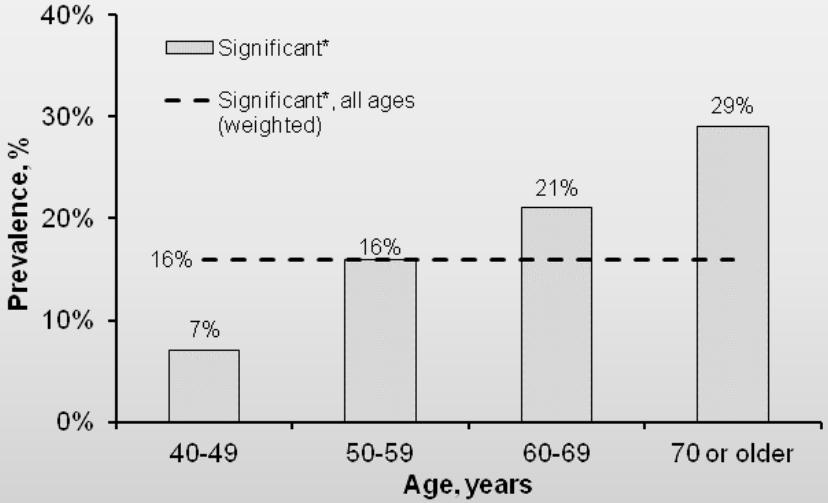
Reference

1. Holden CA et al. *Lancet* 2005; 366: 218–24.

LUTS is more common and more severe as men age[1,2]

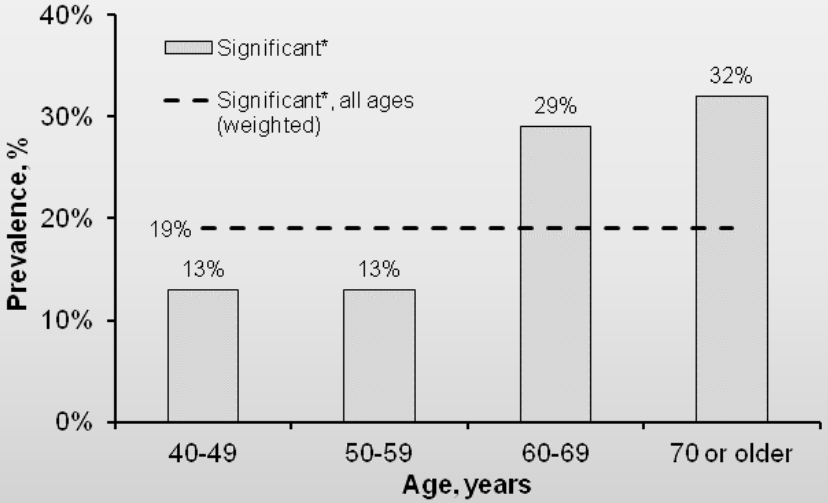
LUTS prevalence, men aged ≥ 40 years in Australia[1]

Holden et al. 2005: Sample of 4,986[1]



*International Prostate Symptom Score ≥ 8.
LUTS, lower urinary tract symptoms.
Adapted from Holden et al. 2005.[1]

Martin et al. 2011: Sample of 990[2]

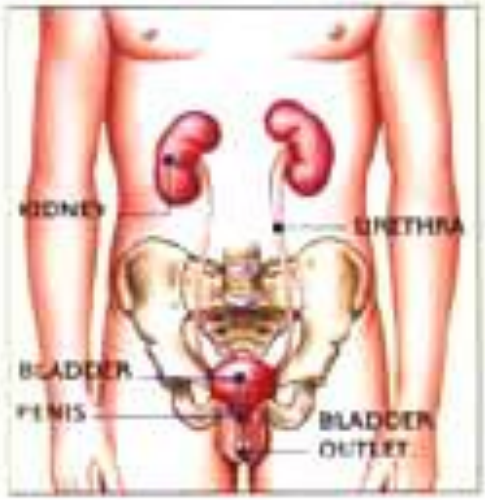


*International Prostate Symptom Score ≥ 8.
LUTS, lower urinary tract symptoms.
Adapted from Martin et al. 2011.[1]

References

1. Holden CA et al. *Lancet* 2005; 366: 218–24.
2. Martin SA et al. *World J Urol* 2011; 29: 179–84.

Male pelvic organs



SPINE

SEMINAL VESICLES

EJACULATORY DUCT

PROSTATE

RECTUM

URINARY BLADDER

PELVIC FLOOR MUSCLE

PUBIC SYMPHYSIS

ANAL SPHINCTER

URETHRA

ANUS

PENIS

COWPER'S GLAND

FORESKIN

VAS DEFERENS

EPIDIDYMIS

BLADDER OUTLET

TESTIS

SCROTUM

URINARY SPHINCTER

The Continence Foundation
307 Hutton Square
16 Baldwin Gardens
London EC1N 7RJ

ED: independently associated with lower urinary tract symptoms[1]

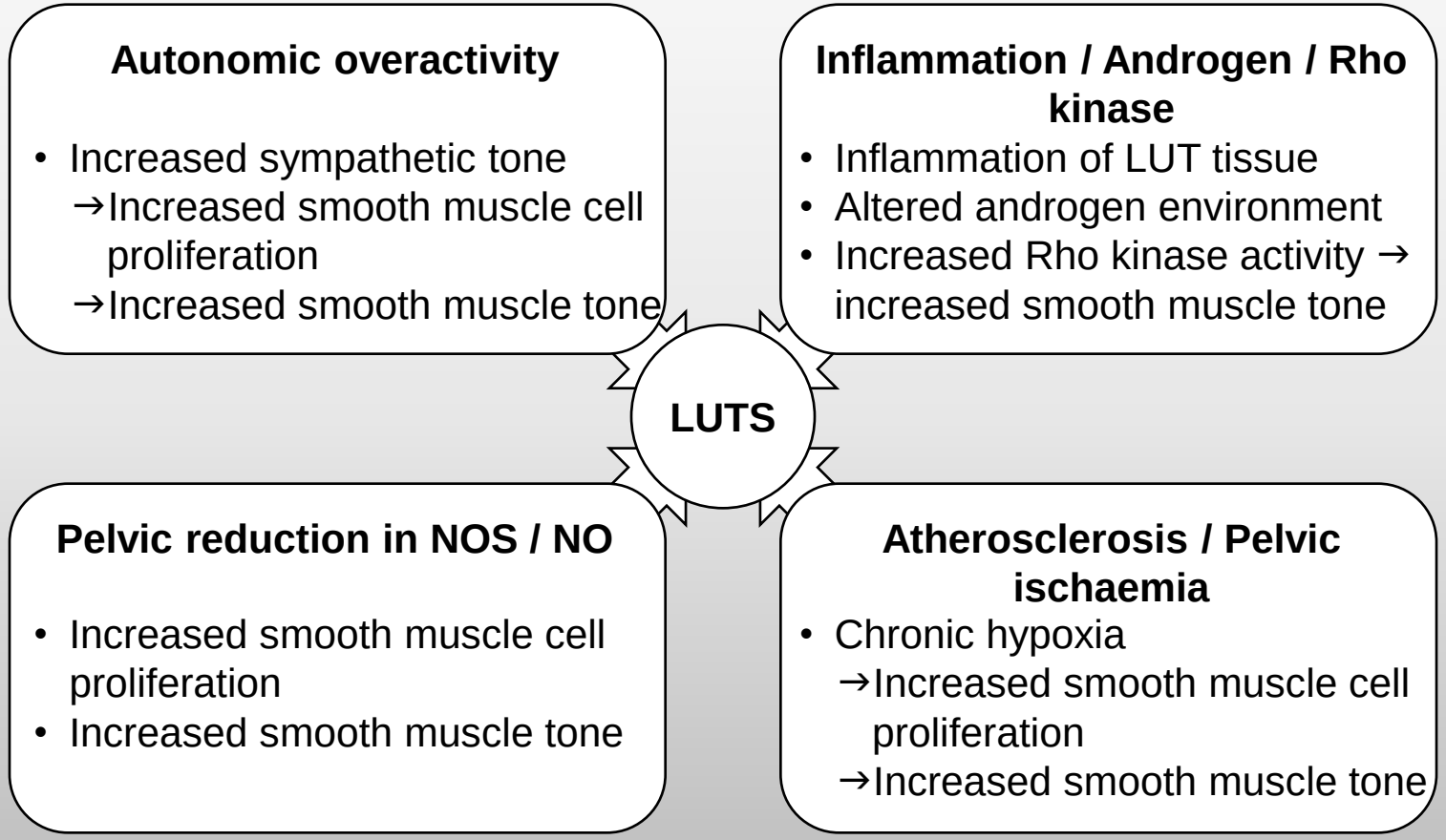
Prostate Symptom Score* quartile (score range)	Adjusted odds ratio†	95% confidence interval
1st (0–3)	Reference	–
2nd (4–7)	1.44	0. 56–3.70
3rd (8–15)	3.45	1.22–9.77
4th (> 15)	3.76	1.29–11.00
Overall	1.05	1.02–1.13 (p=0.01)

*International Prostate Symptom Score. †Odds ratio adjusted for age, education, excessive consumption of alcoholic beverages, smoking, sedentary lifestyle, fasting blood glucose, dyslipidemia, hypogonadism, general obesity (body mass index) and visceral obesity (waist–hip index, sagittal abdominal diameter and waist circumference).

Reference

1. Rhoden EL et al. *J Sex Med* 2008; 5: 2662–8.

The proposed pathophysiology of LUTS is complex[1]



References

1. Andersson KE et al. *Neurourol Urodyn* 2011; 30(3): 292–301.

LUTS, BPH, BOO

- Frequency
- Urgency
- Post micturation dribbling
- Intermittency of flow
- Incomplete emptying
- Reduced flow rate
- Hesitancy
- Nocturia
- Retention

International Prostate Symptom Score (IPSS)*

	Not at all	Less than one time in five	Less than half the time	About half the time	More than half the time	Almost always	Your Score
Incomplete emptying *In the past month, how often have you had a sensation of not emptying your bladder completely after you finish urinating?*	0	1	2	3	4	5	
Frequency	0	1	2	3	4	5	
Intermittency	0	1	2	3	4	5	
Urgency	0	1	2	3	4	5	
Weak Stream	0	1	2	3	4	5	
Straining	0	1	2	3	4	5	
Nocturia	0	1	2	3	4	5	
TOTAL SCORE (MAX 35)							

IPSS

- Max score 35
- Quality of life score - 1 to 5

LUTS treatment

- Alpha blockers
  - Doxazosin
  - Terazosin
  - Tamsulosin
  - Finesteride
- Surgery
  - TURP
  - BNI
  - Laser enucleation
  - Open simple prostatectomy
- Catheter

CIALIS® (tadalafil) for ED and LUTS/BPH

PDE5 inhibitor tadalafil as an OAD therapeutic option for LUTS

All pivotal trials had identical design[1-4]

- Randomised, double-blind, placebo-controlled trials

- Common eligibility criteria includes:
  - Age ≥ 45 years
  - LUTS/BPH > 6 months
  - IPSS ≥ 13 at start of placebo lead-in period
  - Q_{max} 4–15 ml/s

- Common efficacy parameters:
  - International Prostate Symptom Score (IPSS), incl. sub-scores
  - BPH-Impact Index (BII)
  - IIEF Questionnaire (with specific focus on EF-Domain) in sexually active men with ED

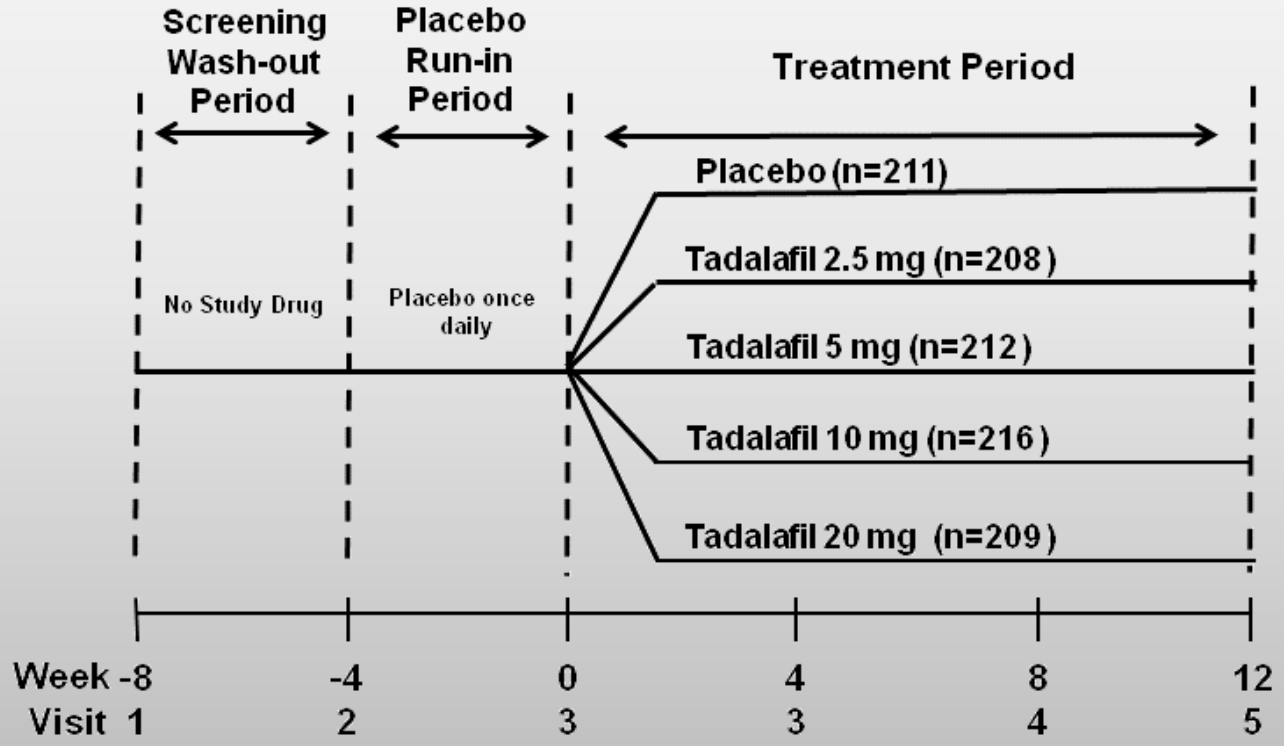
Safety was analysed by treatment-emergent adverse events (TEAEs), laboratory measures, post-void residual urine, and maximum urinary flow rate (Q_{max})

References

1. Roehrborn CG et al. *J Urol* 2008; 180: 1228–34.
2. Porst H et al. *Eur Urol* 2011; 60: 1105–13.
3. Egerdie RB et al. *J Sex Med* 2012; 9: 271–81.
4. Oelke M et al. *Eur Urol* 2012; 61: 917–25.

Tadalafil in LUTS/BPH: Dose-finding[1]

- 1,058 men equally randomised to placebo, 2.5, 5, 10 or 20 mg once-daily

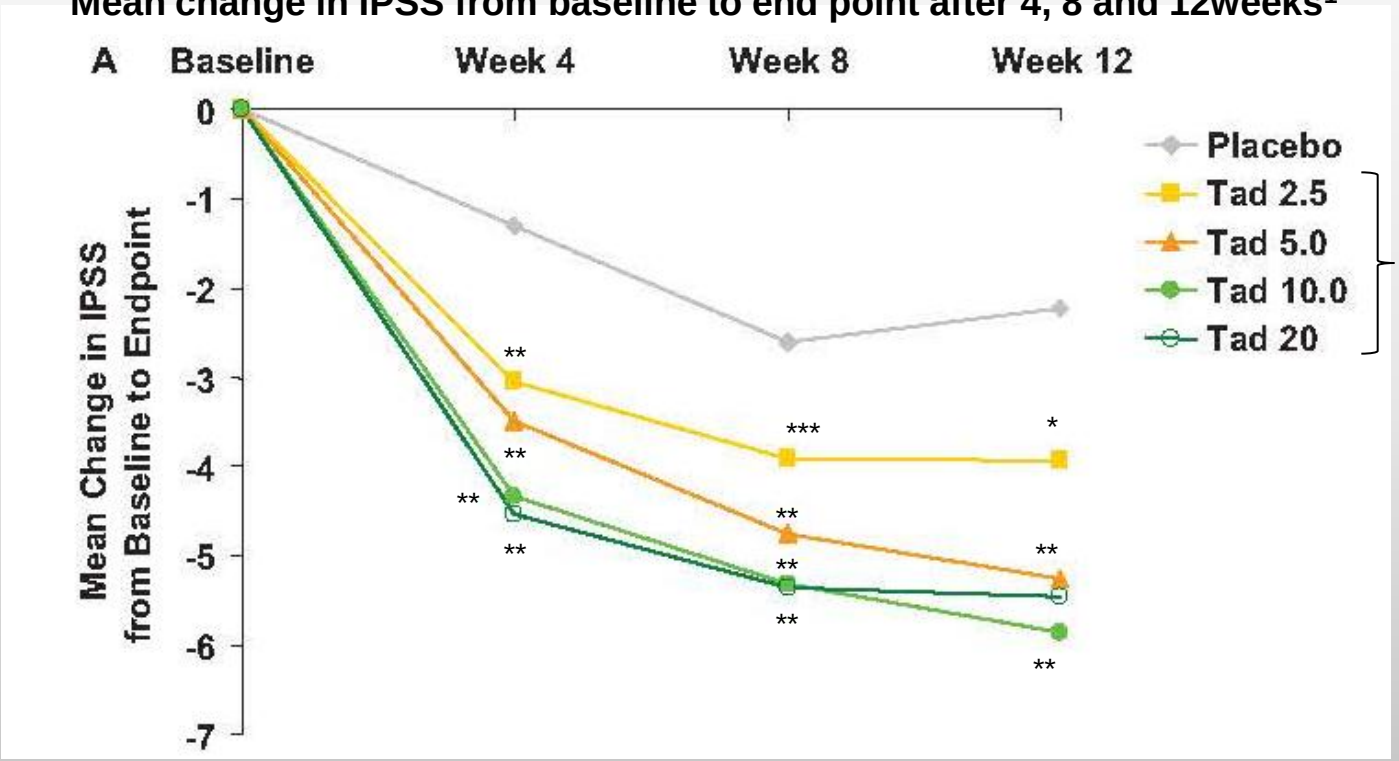


References

1. Roehrborn CG et al. *J Urol* 2008; 180: 1228–34.

CIALIS 5 mg once-a-day chosen for further clinical development

Mean change in IPSS from baseline to end point after 4, 8 and 12weeks[1]



***p < 0.01. **p < 0.001. ***p= 0.028**
IPSS, International Prostate Symptom Score.
Adapted from Roehrborn et al. 2008.[1]

Reference

1. Roehrborn CG et al. *J Urol* 2008; 180: 1228–34.

CIALIS 5 mg once-a-day is well tolerated[1]

	Placebo (n=211)	CIALIS 5 mg (n=212)	CIALIS Total* (n=846)
	n (%)	n (%)	n (%)
Subjects reporting ≥1 TEAE	45 (21.2)	65 (30.7)	279 (33.0)
TEAEs in ≥ 2% of subjects, any treatment group			
Headache	6 (2.8)	6 (2.8)	29 (3.4)
Dyspepsia	0 (0.0)	10 (4.7)	28 (3.3)
Back pain	1 (0.5)	2 (0.9)	27 (3.2)
Myalgia	0 (0.0)	3 (1.4)	18 (2.1)
Nasopharyngitis	2 (0.9)	4 (1.9)	18 (2.1)
Diarrhea	3 (1.4)	6 (2.8)	14 (1.7)
Gastroesophageal reflux disease	0 (0.0)	2 (0.9)	13 (1.5)
Pain in extremity	0 (0.0)	5 (2.4)	13 (1.5)
Bronchitis	1 (0.5)	1 (0.5)	9 (1.1)
Muscle spasms	0 (0.0)	0 (0.0)	9 (1.1)
Subjects with ≥ 1 Serious AE	6 (2.8)	1 (0.5)	11 (1.3)
Subjects discontinued due to AE	5 (2.4)	12 (5.7)	41 (4.8)

*All doses: 2.5 mg, 5 mg, 10 mg and 20 mg

Adapted from Roehrborn et al. 2008.[1]

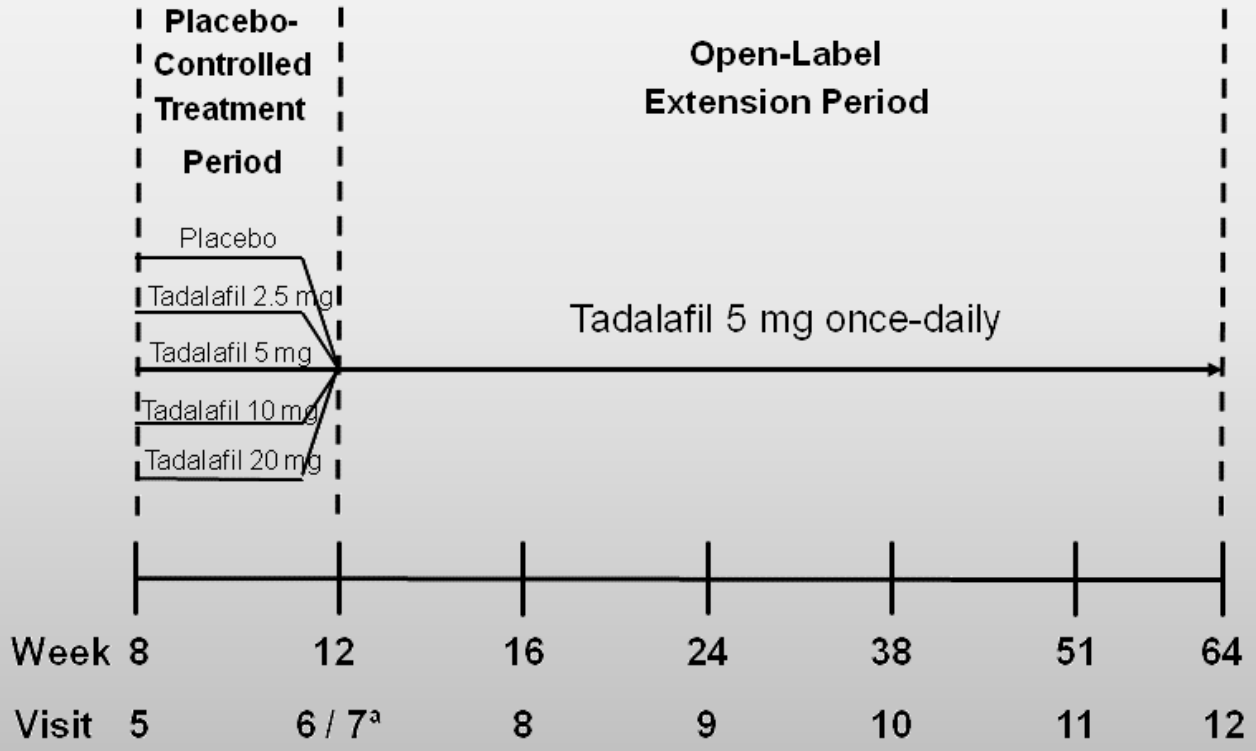
Reference

1. Roehrborn CG et al. *J Urol* 2008; 180: 1228–34.

Please review the full CIALIS Data Sheet for a complete list of contraindications, precautions and interactions

12 month open-label extension trial[1]

- 428 men entered the trial after 12 weeks



[a]Visit 7 occurred within 0- 3 days following the completion of Visit 6.

References

1. Donatucci CF et al. *BJU Int* 2011; 107: 1110–6.

12 month open-label extension trial: Safety[1]

	CIALIS Total* (n=846) n (%)
Subjects reporting ≥1 TEAE	246 (57.6)
TEAEs in ≥ 2% of subjects, any treatment group	
Dyspepsia	17 (4.0)
Gastroesophageal reflux disease	17 (4.0)
Back pain	16 (3.7)
Headache	13 (3.0)
Sinusitis	12 (2.8)
Hypertension	11 (2.6)
Cough	9 (2.1)
Subjects with ≥ 1 Serious AE	20 (4.7)
Subjects discontinued due to AE	22 (5.2)

NOTE: Most TEAEs were mild or moderate in severity. **Adapted from Donatucci et al. 2011.[1]**

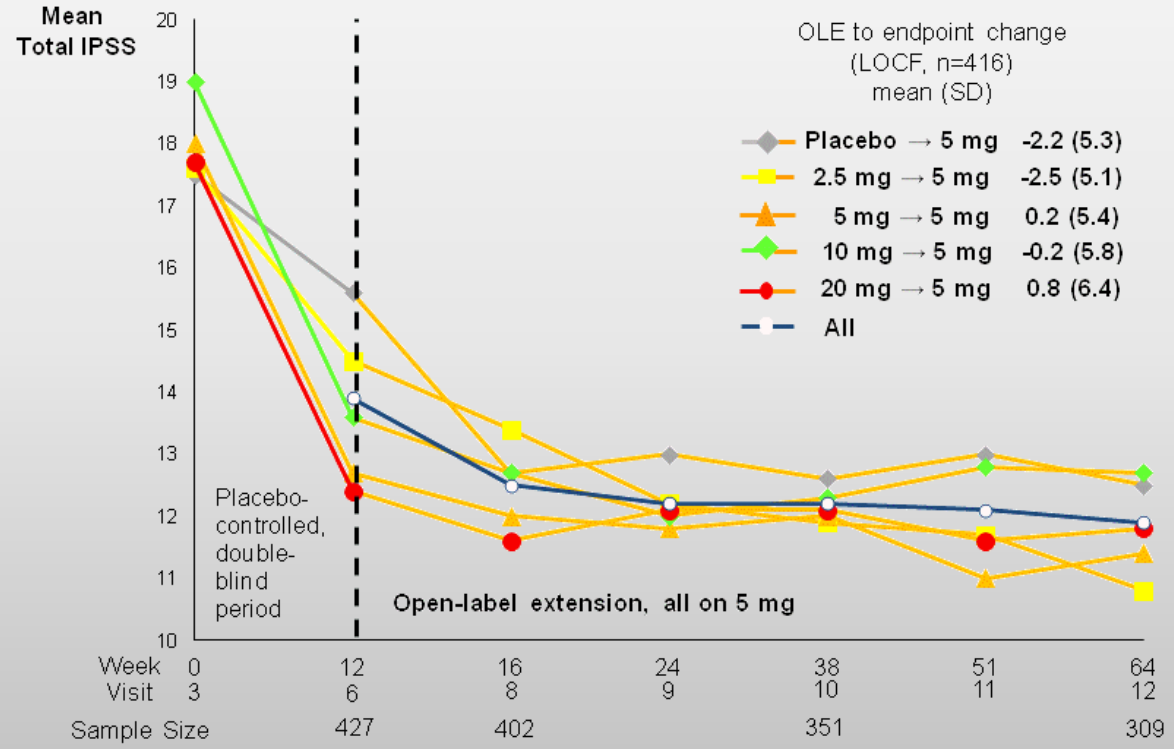
Please review the full CIALIS Data Sheet for a complete list of contraindications, precautions and interactions

Reference

1. Donatucci CF et al. *BJU Int* 2011; 107: 1110–6.

12 month open-label extension trial: Maintenance of effect[1]

Mean change in IPSS from baseline to end point after open-label extension[1]



IPSS, International Prostate Symptom Score. LOCF, last observation carried forward. SD, standard deviation.
Adapted from Donatucci et al. 2011.[1]

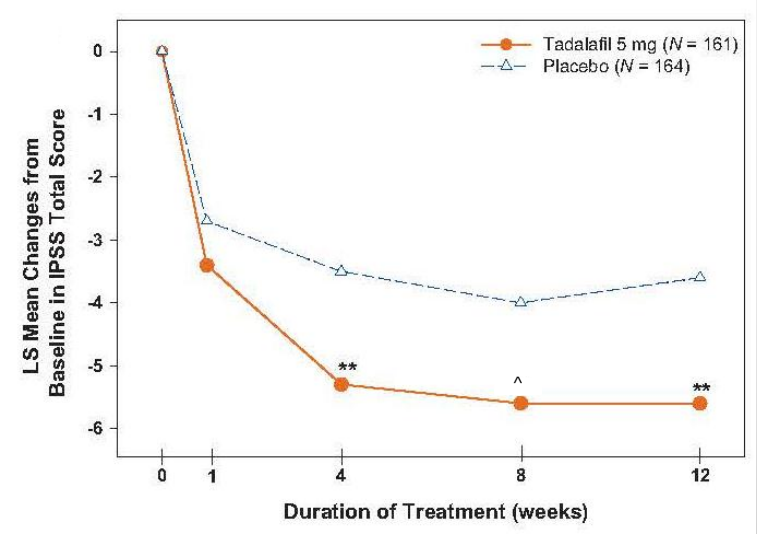
Reference

1. Donatucci CF et al. *BJU Int* 2011; 107: 1110–6.

Confirmation of tadalafil 5 mg once-a-day for LUTS/BPH[1]

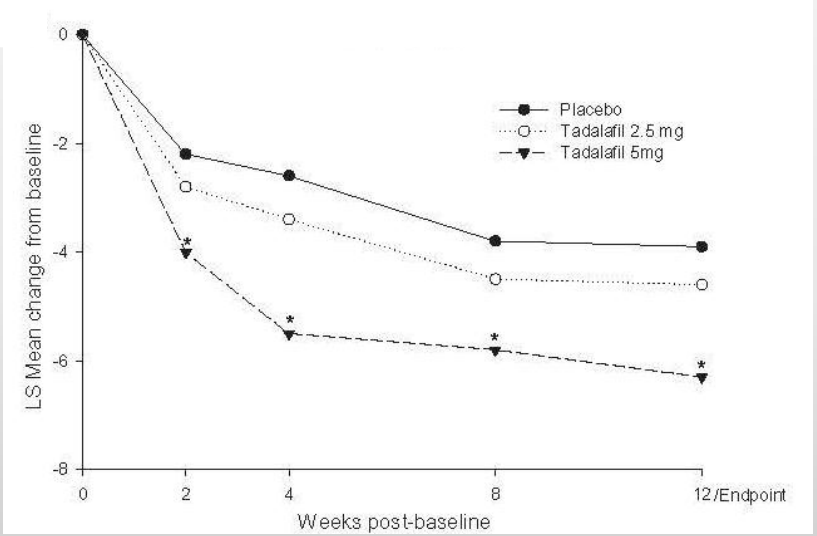
Mean change in total IPSS from baseline to end point[1,2]

Porst et al. 2011: Dose-confirmation[1]



****p < 0.01. ^p < 0.05.**
IPSS, International Prostate Symptom Score.
LS, lean squares.
Adapted from Porst et al. 2011.[1]

Egerdie et al. 2012: Comorbid ED + LUTS[2]



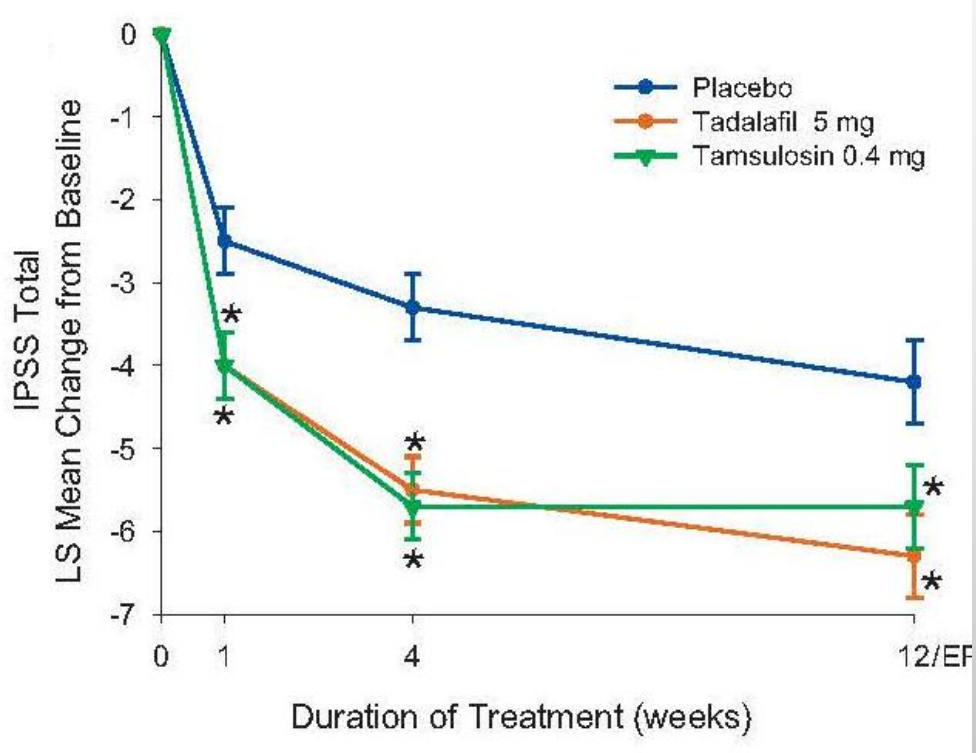
***p < 0.001.**
IPSS, International Prostate Symptom Score.
LS, lean squares.
Adapted from Egerdie et al. 2012.[1]

Reference

1. Porst H et al. *Eur Urol* 2011; 60: 1105–13.
2. Egerdie RB et al. *J Sex Med* 2012; 9: 271–81.

Both tadalafil 5 mg once-a-day and tamsulosin improve IPSS[1]

Mean change in IPSS from baseline to end point[1]

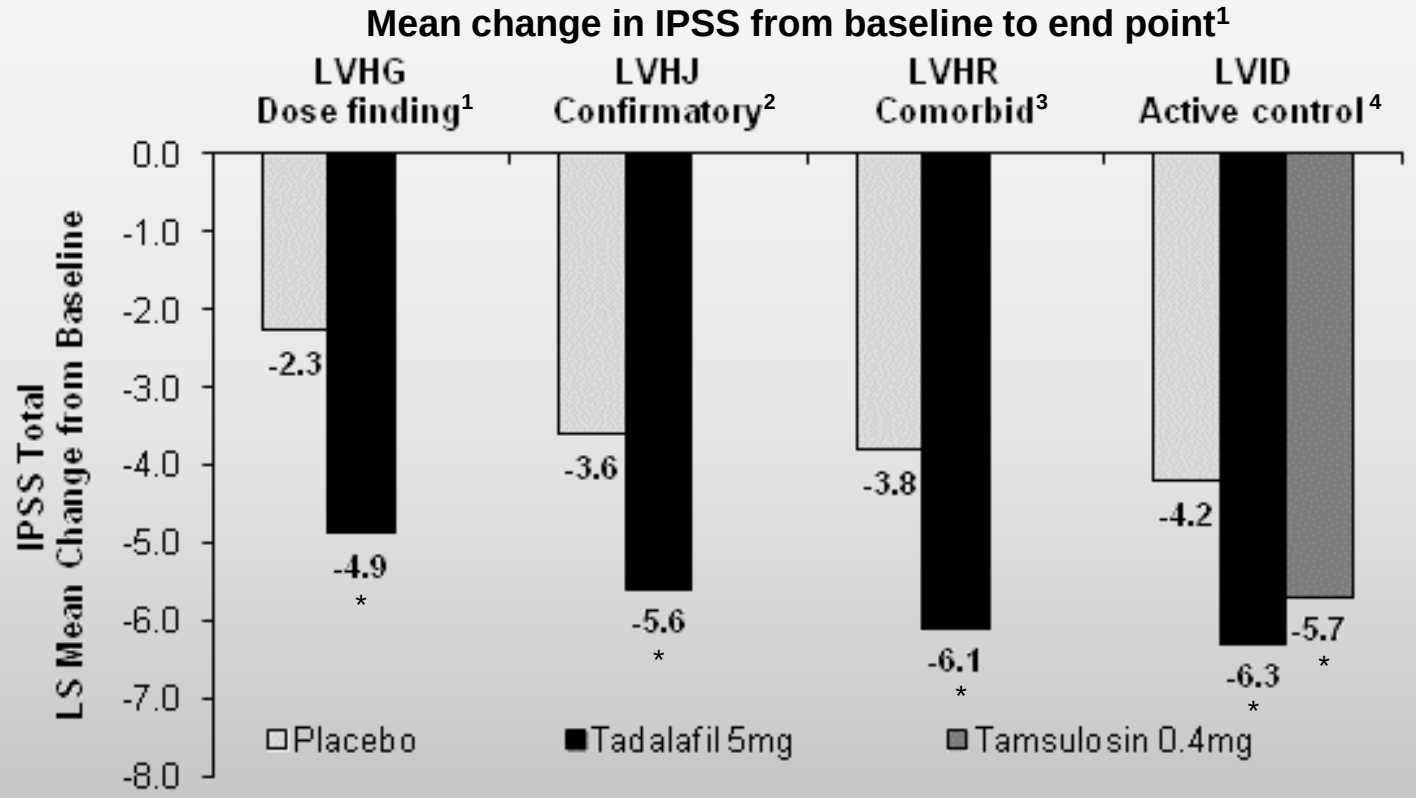


***p < 0.05 versus placebo.**
IPSS, International Prostate Symptom Score. LS, lean squares.
Adapted from Oelke et al. 2012.[1]

Reference

1. Oelke M et al. *Eur Urol* 2012; 61: 917–25.

Consistent Improvement of LUTS across pivotal trials[1-4]



*p < 0.05 versus placebo.
IPSS, International Prostate Symptom Score. LS, lean squares.

Reference

1. Roehrborn CG et al. *J Urol* 2008; 180: 1228–34.
2. Porst H et al. *Eur Urol* 2011; 60: 1105–13.
3. Egerdie RB et al. *J Sex Med* 2012; 9: 271–81.
4. Oelke M et al. *Eur Urol* 2012; 61: 917–25.

Randomised studies stratified according to ED status[1-3]

Erectile Dysfunction prevalence in LVHG, LVHJ and LVID subjects

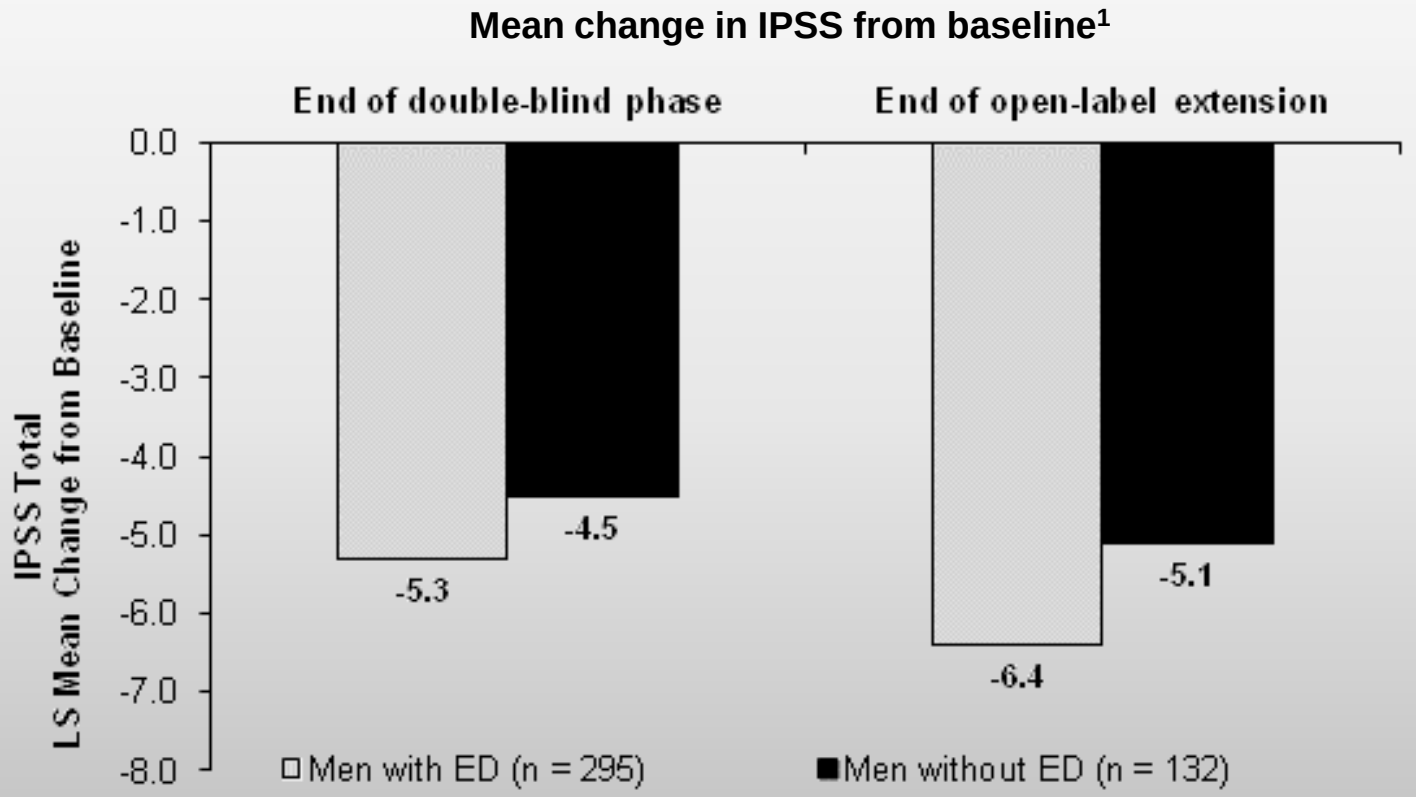
Study	Erectile Dysfunction		No Erectile Dysfunction	
	N	%	N	%
LVHG: Dose-finding[1]	716	67.8	340	32.2
LVHG OLE: Long-term safety[4]	295	69.1	132	30.9
LVHJ: Confirmatory[2]	224	68.9	101	31.1
LVID: Active control[3]	357	69.9	154	30.1
Total	**1,592**	**68.6**	**727**	**31.4**

- For each randomised study, stratification occurred according to diagnosis of erectile dysfunction, baseline LUTS severity, and geographic region.[1-3]

Adapted from the following references:

1. Roehrborn CG et al. *J Urol* 2008; 180: 1228–34.
2. Porst H et al. *Eur Urol* 2011; 60: 1105–13.
3. Oelke M et al. *Eur Urol* 2012; 61: 917–25.
4. Donatucci CF et al. *BJU Int* 2011; 107: 1110–6.

IPSS improvement in men with or without ED[1]



IPSS, International Prostate Symptom Score. ED, Erectile Dysfunction.
LS, lean squares.
Adapted from Donatucci et al. 2011.[1]

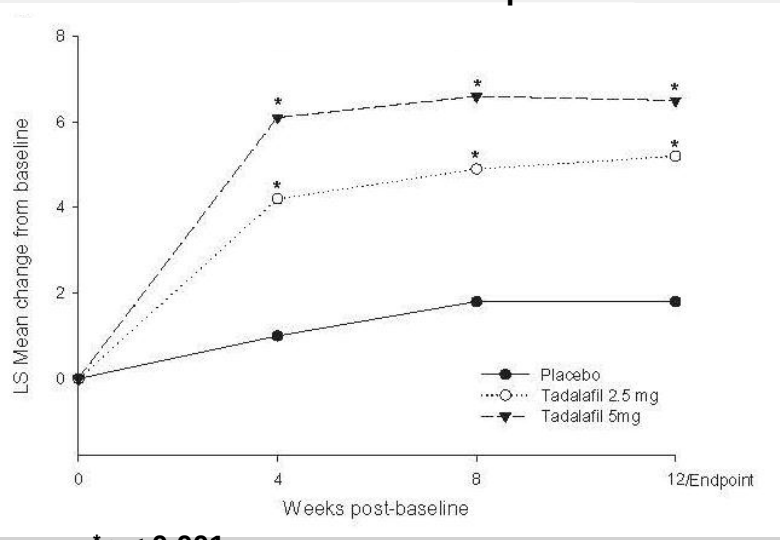
Reference

1. Donatucci CF et al. *BJU Int* 2011; 107: 1110–6.

Treatment of both conditions in men with ED and LUTS/BPH[1]

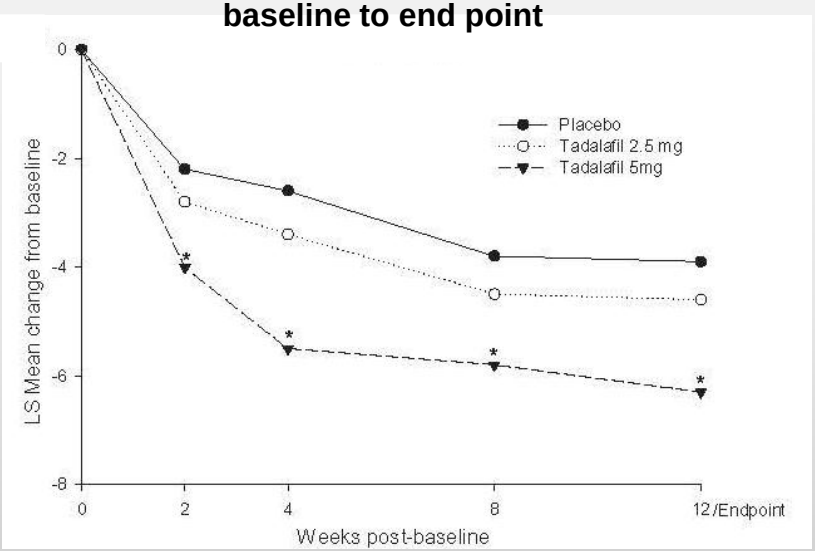
Egerdie et al. 2012: Comorbid ED + LUTS/BPH[1]

Mean change in IIEF-EF domain from baseline to end point



*p < 0.001.
IIEF, International Index of Erectile Function-Erectile Function. LS, lean squares.
Adapted from Egerdie et al. 2012.[1]

Mean change in total IPSS from baseline to end point



*p < 0.001.
IPSS, International Prostate Symptom Score. LS, lean squares.
Adapted from Egerdie et al. 2012.[1]

Reference

1. Egerdie RB et al. *J Sex Med* 2012; 9: 271–81.

Safety and tolerability for CIALIS OAD in LUTS/BPH[1]

TEAEs reported by ≥ 2% of patients treated with tadalafil 5 mg for LUTS/BPH and more frequent on drug than placebo in phase III studies

System organ class	Adverse event	CIALIS (n=752) %	Placebo (n=748) %
Nervous system	Headache	3.9	2.0
Musculoskeletal and connective tissue disorders	Back pain	2.4	1.2
Gastrointestinal disorders	Dyspepsia	2.4	0.1

Please review the full CIALIS Data Sheet for a complete list of contraindications, precautions and interactions

Reference

1. CIALIS Data Sheet. Date of preparation: 31 January 2013.

Key messages

- Similar design of all pivotal clinical studies of CIALIS in LUTS/BPH[1-4]
- 52 week open-label extension study demonstrated:
  - Long-term tolerability and safety[5]
  - Maintenance of effect for CIALIS 5mg once-a-day[5]
- Significant IPSS improvement for patients with LUTS/BPH[1-4]
- Significant proportion of patients with both LUTS/BPH and ED across studies[1-5]
  - CIALIS 5mg once-a-day efficacy in LUTS patients with and without ED[1-5]
- Additional improvement in erectile function in patients with both LUTS/BPH and ED[1-4]

References

1. Roehrborn CG et al. *J Urol* 2008;180:1228–34.
2. Porst H et al. *Eur Urol* 2011;60:1105–13.
3. Egerdie RB et al. *J Sex Med* 2012;9:271–81.
4. Oelke M et al. *Eur Urol* 2012;61:917–25.
5. Donatucci CF et al. *BJU Int* 2011;107:1110–6.

CIALIS® (tadalafil) for ED and LUTS/BPH

Summary

Key messages

- Prevalence and severity of ED increases with age
- ED impacts more than the ability to simply have sex – there is a psychosocial impact
- Compared with sildenafil 100mg PRN, CIALIS 5mg OAD significantly improves sexual self confidence, time concerns and spontaneity in men with ED
- ED is associated with a number of other conditions, including LUTS
  - Similar to ED, the prevalence and severity of LUTS increases with age
  - Although not yet certain, ED and LUTS may share common pathophysiological elements
- CIALIS 5mg OAD is efficacious and well-tolerated in LUTS/BPH patients with and without ED

References

Please refer to the ‘Reference list’ on the last slide of this presentation.

Please review full Approved Product Information before prescribing. The Data Sheet can be accessed at medsafe.govt.nz

Cialis® is an UNFUNDED PRESCRIPTION MEDICINE, for which charges will apply, for the treatment of erectile dysfunction (ED) in men, moderate to severe lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH) and for co-existing ED & LUTS associated with BPH. Tablets contain tadalafil 2.5mg, 5mg, 10mg or 20mg. Maximum daily dose 5mg for continuous daily use. Maximum daily dose 20mg for ondemand use. Sexual stimulation is required for Cialis to work. Do not use when taking nitrates for angina or where there is known unstable heart disease like myocardial infarction, heart failure or heart rhythm disturbances, low or uncontrolled blood pressure, or recent history of stroke. Do not use if loss of vision in one eye from nonarteritic anterior ischaemic optic neuropathy (NAION). Caution in severe kidney or liver disease or conditions which predispose to pirapism. Caution with pre-existing CV disease, use in combination with anti-hypertensives and other ED treatment. Discontinue if sudden loss of vision (one or both eyes) or sudden decrease or loss of hearing. Not to be used by women. Possible side effects include headache, dyspepsia, back & muscle pain, pain in extremity, nasal congestion flushing, dizziness, gastroesophageal reflux, diarrhoea, abdominal pain, upper respiratory tract infection. Before prescribing please review full Approved Product Information. Full PI is available from Eli Lilly. For further product information check the Data Sheet on www.medsafe.govt.nz or call 0800 CIALIS / 242547. Eli Lilly, Auckland. TAPS CH3598 NZCLS00151.

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- VIAGRA Data Sheet. Date of preparation: 22 January 2008.