Clinical Study Synopsis

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The study listed may include approved and non-approved formulations or treatment regimens. Data may differ from published or presented data and are a reflection of the limited information provided here. The results from a single trial need to be considered in the context of the totality of the available clinical research results for a drug. The results from a single study may not reflect the overall results for a drug.

Bayer HealthCare

Clinical Trial Results Synopsis

Study Design Description		
Study Sponsor:	Bayer HealthCare AG	
Study Number:	12496	NCT00461123
Study Phase:	II	
Official Study Title:	A randomized, double-blind, parallel group prospective pilot study to assess the effect of vardenafil on clinical outcome and on procedure duration after green light laser-ablation of the prostate gland for therapy of benign prostate hypertrophy (BPH)	
Therapeutic Area:	Men' s Health	
Test Product		
Name of Test Product:	Vardenafil (Levitra, BAY38-9456)	
Name of Active Ingredient:	Vardenafil Hydrochloride (HCL)	
Dose and Mode of Administration:	One tablet of vardenafil 10 mg was taken orally the evening before ablation of prostate, a second tablet of vardenafil 20 mg was taken orally approximately one hour before ablation of prostate commenced. The stated dose refers to vardenafil base.	
Reference Therapy/Placebo		
Reference Therapy:	Placebo	
Dose and Mode of Administration:	One matching placebo tablet was taken orally the evening before ablation of prostate, a second matching placebo tablet was taken orally approximately one hour before ablation of prostate commenced.	
Duration of Treatment:	Two single doses on two consecutive days of either test drug or placebo.	
Studied period:	Date of first subjects' first visit:	19 MAR 2007
	Date of last subjects' last visit:	02 JUN 2008
Premature Study Suspension / Termination:	No	
Substantial Study Protocol Amendments:	Amendment no. 1 (dated 23 JAN 2007) specified the addition of congestive heart failure (NYHA III, IV) to exclusion criterion concerning heart disease.	
Study Centre(s):	The study was conducted at a single center in Germany.	
Methodology:	This mono-center, randomized, double-blind, parallel-group, placebo-cotrolled, fixed dose study comprised of 5 visits: Visit 1 (treatment with study drug 1 day before surgery), Visit 2 (surgery and treatment with study medication), Visit 3 (1 day post-surgery), Visit 4 (approximately 45 days post-surgery), and Visit 5 (approximately 90 days post-surgery). The primary endpoint peak urinary flow was assessed at Visits 1, 4, and 5. For secondary endpoints subjects were asked to fill International Prostate Symptom Score (IPSS) questionnaire on Visits 1, 4, and 5. Urodynamics were assessed prior to surgery (Visit 1) vs 90 days post-surgery (Visit 5) by means of diary cards which subjects had to fill in at weekly intervals. Data regarding adverse events were collected at all visits after Visit 1.	

Indication/ Main Inclusion Criteria:	Indication: BPH Main Inclusion Criteria: Men with BPH requiring surgical treatment, up to 80 years of age. Not eligible with a history of surgical prostatectomy, suspicion of prostate cancer, or severe cardiovascular condition including unstable angina pectoris and congestive heart failure, but transurethral intervention was allowed.
Study Objectives:	Overall: To compare the impact of vardenafil application vs. placebo on Greenlight® laser ablation of the prostate in patients presenting with BPH. Primary: The primary objective of this study was to compare the efficacy of 10 mg + 20 mg vardenafil ingested prior to laser prostate ablation versus placebo and 90 days after surgery with regard to increased peak urinary flow (Q_{max}). Secondary: • Duration of surgery • Post-void residual (PVR) volume, time frame up to 3 months after surgery • Number of weekly incontinence episodes (patient diary) • International Prostate Symptom Score (IPSS) total score
Evaluation Criteria:	Efficacy (Primary): • Change in peak urinary flow (Q_{max}), time frame up to 3 months after surgery Efficacy (Secondary): • Duration of surgery • Decrease in post-void residual (PVR) volume pre vs post-ablation of prostate (after 3 months of surgery) assessed by means of ultrasonography • The required duration of laser application expressed by the overall energy (in joule) administered during the entire duration of surgery. The applied energy correlates to 100% with the duration application of the Greenlight® laser • Number of micturitions per week (if any) prior to ablation of prostate vs 3 months after surgery, as reported by the subject by means of a diary card (filled at weekly intervals) • Number of urgency episodes per week prior to ablation of prostate vs 3 months after ablation as reported by the subject by means of a diary card (filled at weekly intervals) • Number of incontinence episodes per week prior to ablation of prostate vs 3 months after ablation as reported by the subject by means of a diary card (filled at weekly intervals) • Number of nycturias per week prior to ablation of prostate vs 3 months after ablation as reported by the subject by means of a diary card (filled at weekly intervals) as reported by the subject by means of a diary card (filled at weekly intervals)

	• IPSS total score before ablation of prostate vs 3 months postoperatively • IPSS "irritative" sub-score before ablation of prostate vs 3 months postoperatively • IPSS "obstructive" sub-score before ablation of prostate vs 3 months postoperatively • IPSS QoL assessment before ablation of prostate vs 3 months postoperatively Safety: • Adverse events, laboratory, vital signs, and electrocardiogram (ECG)
Statistical Methods:	Efficacy (Primary): Mean values and changes from baseline for the following variables were analyzed using descriptive statistics: baseline adjusted Q_{max} measurement 3 months after surgery in the intent-to-treat (ITT) population. Confirmatory analysis of covariance (ANCOVA) was conducted using baseline values as covariate and the final or last observation carried forward (LOCF) value as dependent variable. Efficacy (Secondary): Mean values and changes from baseline for the following variables were analyzed using descriptive statistics: duration of surgery, volume of residual urine, numbers of weekly incontinence episodes (patient diary), and IPSS total score. Exploratory ANCOVAs/ANOVAs were conducted on the ITT population. Safety: Safety parameters were tabulated using descriptive statistics by treatment group. Adverse events were coded following Medical Dictionary for Regulatory Activities (MedDRA), Version 11.1.
Number of Subjects:	Planned: 50 subjects. Analyzed: 50 subjects, 25 randomized to vardenafil, 25 to placebo.

Study Results

Results Summary — Subject Disposition and Baseline

All 50 subjects were valid for safety analysis because they took at least one dose of study drug and had any safety follow-up. The ITT population included subjects valid for safety who had undergone surgery, whose type of surgery (Greenlight® laser-ablation) had not changed, with energy consumption during surgery reported, and who had taken their second dose of study drug on the day of surgery; it comprised of 21 subjects in the placebo group and 23 subjects in the vardenafil group. Per-protocol (PP) population included 18 subjects in the vardenafil group and 17 subjects in the placebo group.

All subjects were White with mean age of 65.9 years (range: 48.0 to 79.0). Mean body mass index was 26.7 Kg/m^2 (range: 19.3 to 35.4).

Results Summary — Efficacy

Primary efficacy:

The peak urinary flow data were rather similar at baseline and Day +90, adjusted improvements being about 15 mL/s in each treatment group. There was no statistically significant difference between treatments in ANCOVA (Table 1).

Table 1: Peak urinary flow (Q_{max}; mL/s) change from baseline to Day +90 (ITT)

	Vardenafil 10/20 mg (N=23)	Placebo (N=21)	Difference
Mean ± SD			
Baseline (Day -1)	8.3 ± 4.08	9.4 ± 5.69	
Day +90 (LOCF)	23.1 ± 10.60	25.7 ± 7.90	
Change from Baseline	14.9 ± 10.60	16.3 ± 6.65	N/A
ANCOVA			
Baseline (Day -1) - LS mean	8.27	9.41	
Day +90 (LOCF) - LS mean	23.46	25.39	
Change from Baseline - LS mean	15.19	15.98	
Difference of LS means			1.93
95% confidence interval			-4.18 – +8.05
P value (F-test)			0.5248

SD: standard deviation, LOCF: last observation carried forward,
ANCOVA: analysis of covariance, LS mean: least squares mean

Secondary efficacy:

Duration of surgery (mean ± SD) was 72.5 ± 25.8 minutes for placebo (n=21) and 75.1 ± 36.5 minutes for vardenafil (n=23). The data does not suggest a difference between treatments (exploratory F-test).

Change from baseline to Day +90 (LOCF) in PVR volume was -94.8 ± 75.66 mL for placebo (n=17) and -120.6 ± 110.01 mL for vardenafil (n=18). The data does not suggest a difference between treatments (exploratory F-test).

Change from baseline to Day +90 (LOCF) in the number of urinary incontinence episodes was +0.4 ± 1.42 for placebo (n=18) and -1.2 ± 28.37 for vardenafil (n=17). The data may suggest a reduction in the number of urinary incontinence episodes following treatment with vardenafil vs placebo (exploratory F-test: P = 0.0588).

Change from baseline to Day +90 (LOCF) in IPSS total score was -13.0 ± 6.16 mL for placebo (n=19) and -12.2 ± 7.30 mL for vardenafil (n=20). The data does not suggest a difference between treatments (exploratory F-test).

Results Summary — Safety

Ingestion of study drug was controlled by medical staff. Few adverse events occurred after initiation of study within 30 days after second (last) dose. Treatment-emergent adverse events were recorded for 1 subject (4%) in the placebo group and for 3 subjects (12%) in the vardenafil group (Table 2).

Table 2: Incidence rates of adverse events (Safety)

Number of subjects (%)	Vardenafil 10/20 mg (N=25)	Placebo (N=25)
Treatment emergent adverse events (including serious)	3 (12%)	1 (4%)
Drug-related treatment emergent adverse events	1 (4%)	0 (0%)
Treatment emergent adverse events leading to discontinuation	1 (4%)	0 (0%)
Treatment emergent serious adverse events	1 (4%)	2 (8%)
Drug-related treatment emergent serious adverse events	0 (0%)	0 (0%)
Serious adverse events with outcome death	0 (0%)	0 (0%)

One subject in the vardenafil group had a serious adverse event (prostate cancer). Two subjects in the placebo group had serious adverse events (urinary retention; bladder transitional cell carcinoma). None of these events were considered to be related to study drug. One subject receiving vardenafil developed flushing which, according to the investigator, was related to study drug and thus required premature discontinuation of treatment.

There was no evidence of any clinically relevant findings in terms of vital signs and safety laboratory. ECG was only assessed prior to administration of study medication. No follow-up has been documented in conjunction with the study.

Conclusion(s)

This study gave no evidence that administration of vardenafil shortly before conduct of Greenlight® laser-ablation of the prostate exerts an effect on the duration of surgery; consequently, no clinically significant effect on the clinical outcomes could be expected. In particular, an increased peak urinary flow (Q_{max}; primary variable) was not observed. Evaluation of safety in this small sample did not reveal any new or relevant findings.

Publication(s):	None		
Date Created or Date Last Updated:	25 APR 2012	Date of Clinical Study Report:	30 OCT 2009

Investigational Site List

Marketing Authorization Holder in Germany	
Name	Bayer Pharma AG
Postal Address	D-51368 Berlin Deutschland
Sponsor in Germany	
Legal Entity Name	Bayer HealthCare AG
Postal Address	D-51368 Leverkusen, Germany

List of Investigational Sites

No	Facility Name	Street	ZIP Code	City	Country
1	Universitätsklinikum Heidelberg	Urologische Universitätsklinik Im Neuenheimer Feld 110	69112	Heidelberg	GERMANY

Product Identification Information

Product Type	Drug
US Brand/Trade Name(s)	Levitra, STAXYN
Brand/Trade Name(s) ex-US	Levitra, Vivanza, Yaila, Levitra 10mg orodispersible tablets, STAXYN, Vivanza 10mg orodispersible tablets
Generic Name	Vardenafil
Main Product Company Code	BAY38-9456
Other Company Code(s)	
Chemical Description	Vardenafil: 1-[[3-(3,4-Dihydro-5-methyl-4-oxo-7propylimidazo[5,1-f]-as-triazin-2-yl)-4-ethoxyphenyl]sulfony]-4-ethylpiperazine
Other Product Aliases	

Date of last Update/Change: 18 March 2014