Efficacy and Safety of Teverelix LA, a new GnRH antagonist, in patients with benign prostatic hyperplasia (BPH)

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Teverelix (GnRH antagonist) - History

Over 400 subjects have received over 850 doses of teverelix

No serious adverse events have been reported

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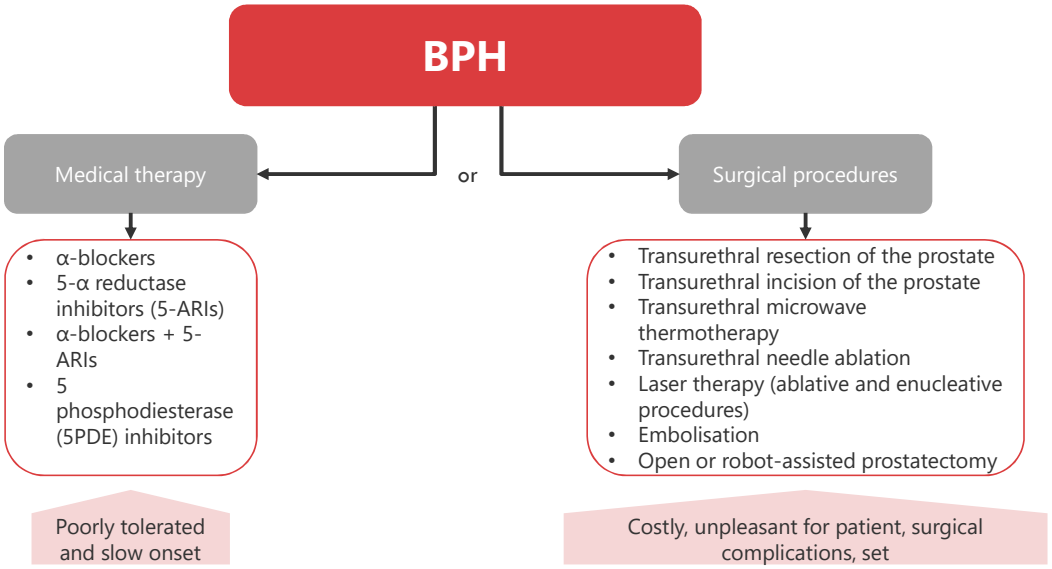
Current BPH Standard of Care



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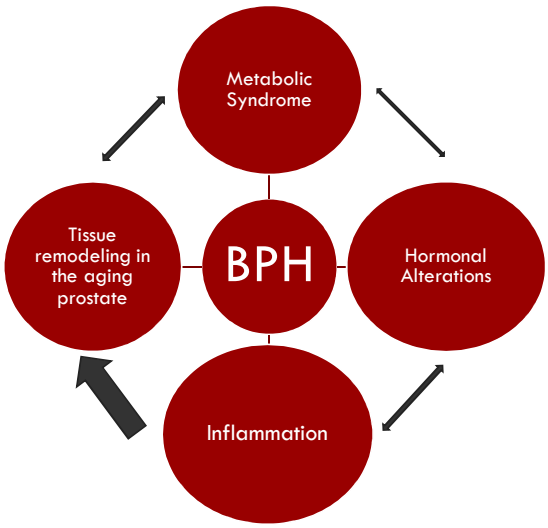
BPH Etiology

BPH is a histological diagnosis associated with unregulated proliferation of connective tissue, smooth muscle and glandular epithelium. Its etiology is multifactorial with the following being identified as risk factors:

- age
- genetics
- sex steroid hormones
- metabolic syndrome
- cardiovascular disease
- obesity
- diabetes
- diet/physical activity
- inflammation



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Study Description

- **A phase II randomized, double-blind, placebo-controlled, multicentre, multinational study investigating two single injections of 60 mg at 48 hours interval administered s.c. to treatment naive patients suffering from BPH**
  - **Study Period: May – Dec 2004**
  - **No. enrolled subjects: 81 (teverelix 41; placebo 40)**

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Investigational Sites

Prof. Dr. F.M.J. Debruyne/Department of Urology, University Hospital Nijmegen, The Netherlands	Co-ordinating Investigator
Dzmitryieu AV, Urology center PRZO Minsk, Belarus	Clinical Investigator
Gres A, MOKB, Clinic of urology, Minsk, Belarus	Clinical Investigator
Strockyi A, 54th City Hospital, Minsk, Belarus	Clinical Investigator
Dovger V, City Emergency Hospital, Minsk, Belarus	Clinical Investigator
Ulys A, Oncology Institute of Vilnius University, Vilnius, Lithuania	Clinical Investigator
Černiauskienė A, Vilnius University Hospital Santariskiu Klinikos, Vilnius, Lithuania	Clinical Investigator
Geavlette P, Spitalul Clinic de Urgentia "Sf.Ioan", Bucharest, Romania	Clinical Investigator
Nikolovski M, Medical University Alexandrovski Hospital,Sofia, Bulgaria	Clinical Investigator

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Study Objectives

- **Primary Objective**
- to investigate the effects of Teverelix LA on symptoms of BPH measured by the International Prostate Symptom Score (I-PSS)

- **Secondary Objectives**
- to assess the effects on:-
  - uroflow (Qmax)
  - prostate volume
  - residual urinary volume
  - testosterone and dihydrotesterone (DHT)
  - safety of Teverelix LA

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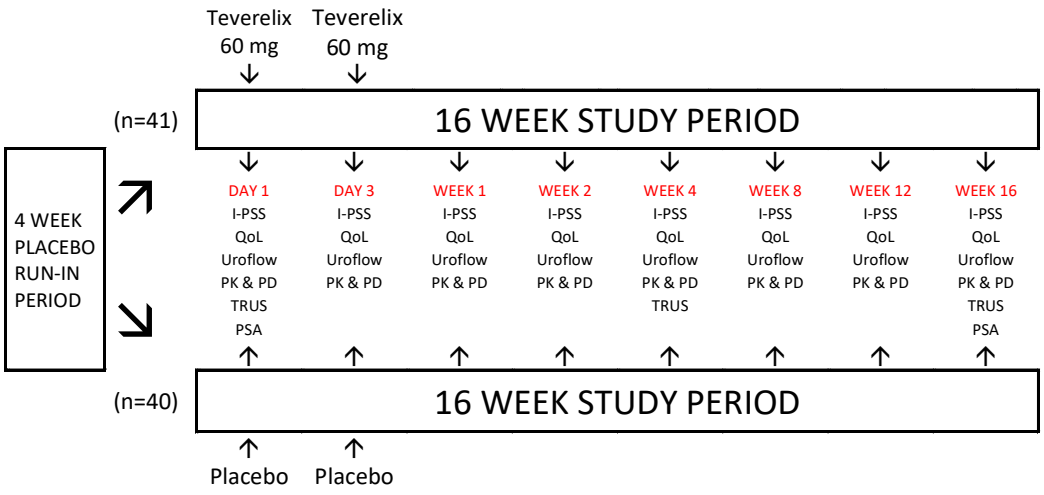
A012 Study Schematic



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Study Population

Eligibility Criteria

- >50 years of age
- Benign Prostatic Hyperplasia
- Bothersome voiding symptoms : I-PSS >13
- Uroflow <13 ml/sec for a voided vol. >150 ml
- Treatment naive

Table 1		
Mean Baseline Data	ITT population	
	Teverelix (n=41)	Placebo (n=40)
Age (years)	67.9	67
I-PSS	18.4 ± 4.6	17.6 ± 4.1
Prostate Volume (cm3)	50.04 ± 23.89	48.35 ± 22.68
PSA (ng/mL)	3.00 + 2.50	2.98 + 2.68
Qmax (mL/sec)	4.96 ± 1.24	5.51 ± 1.39
PVR (mL)	36.99 ± 45.10	37.19 ± 48.09

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A012 trial demonstrates…

Significant reduction in **prostate size** ✓

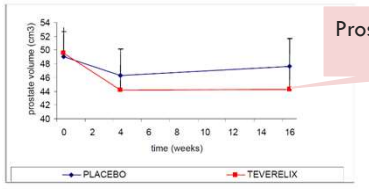

Figure 3: Change in mean prostate size (±SEM)

Prostate volume reduces by 11%

Significant increase in **urine flow** ✓

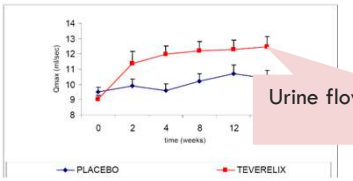

Figure 2: Change in uroflow rate (mean Q_{max})(±SEM)

Urine flow increases by 40%

Significant reduction in **symptoms (I-PSS)** ✓

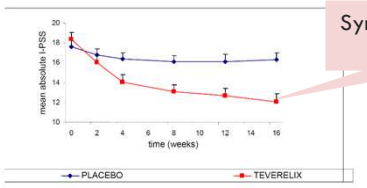

Figure 1: Mean absolute I-PSS score (± SEM)

Symptom score reduces by ≈25%

Reduction in **testosterone** but above castration levels ✓

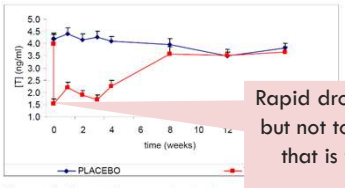

Figure 4: Change in mean testosteron

Rapid drop in testosterone but not to castration level that is then reversed.

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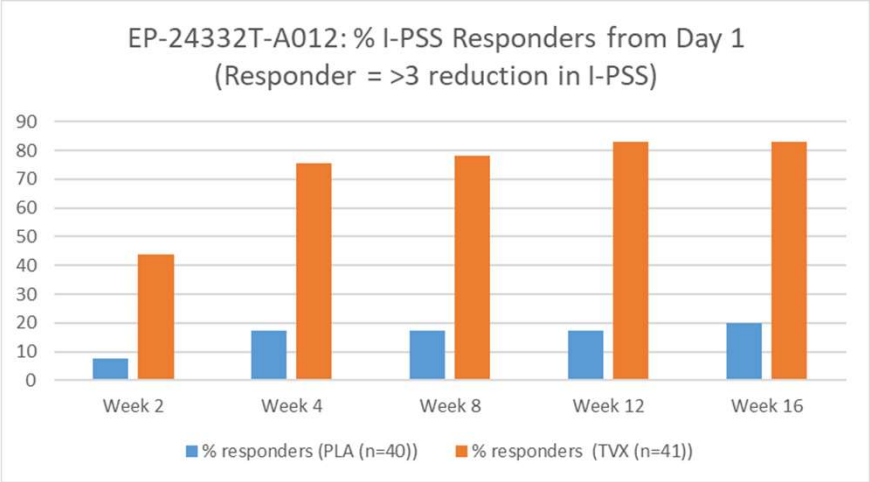
Clinically Relevant Responders

Figure 5



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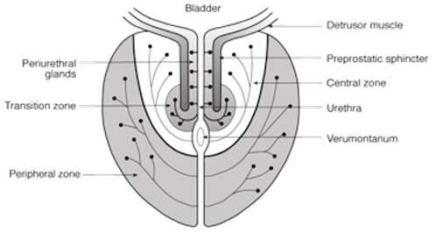
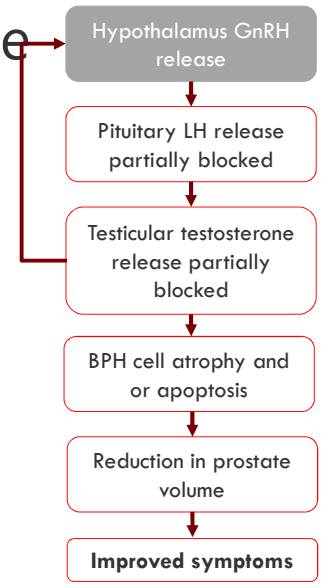
Indirect effect of Teverelix on prostate





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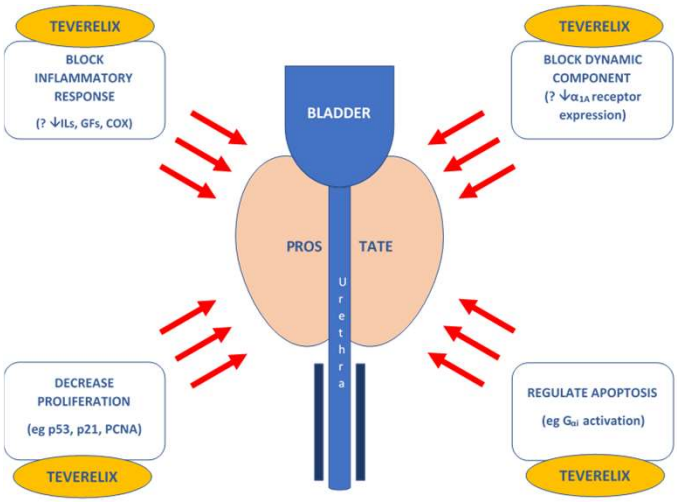
Possible direct effects of Teverelix on prostate



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Summary

- **4 weeks after first administration 44% of teverelix subjects reported a clinically relevant (≥3 point) reduction in I-PSS compared with 8% of placebo subjects**
- This rose to 76% (17.5% placebo) by Week 8 and 83% (17.5% placebo) by Week 12 and was **maintained at Week 16** (83%/20%)

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Summary

- **This compares favourably with results from the COMBAT trial (2008) where, after 24 months of treatment the % of subjects with a ≥3 point reduction in I-PSS were:**
  - **65% Dutasteride (0.5 mg od)**
  - **62% Tamsulosin (0.4 mg od)**
  - **72% Both**

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Conclusions

- Teverelix may offer a novel therapy for the treatment of BPH which may be effective in a greater percentage of the patient population than existing, combination therapies
- Rapid onset of symptom relief alongside alleviation of disease progression could make this an attractive therapy for LUTS-associated BPH
- **Larger, repeat dose clinical trials will be required to consolidate these Phase 2 data**

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