This report may include approved and non-approved uses, formulations, or treatment regimens. The results reported may not reflect the overall profile of a product. Before prescribing any product mentioned in this report, healthcare professionals should consult local prescribing information for the product approved in their country.

Name of company Schering-Plough Research Institute **Name of active substance** Org 3236	**Synopsis / Tabular Format** **referring to**	

Title of the clinical trial

A phase II, randomized, double-blind, placebo-controlled trial investigating the efficacy and safety of Org 3236 tablets in men with Lower Urinary Tract Symptoms (LUTS) suggestive of Benign Prostatic Hyperplasia (BPH).

Clinical Trial Report on Protocol 304001.

Investigator(s)

[redacted]

Centre codes are provided between brackets

Clinical trial center(s)

Argentina

[redacted]

Germany

[redacted]

Report/publication (ref)

Not applicable.

Studied period (years)

April, 2008 – August, 2008

Clinical phase

Phase II

Objectives

The objectives were to evaluate:

- The effect of Org 3236 on prostate volume compared to placebo;
- The effect of Org 3236 on LUTS compared to placebo;
- The effect of Org 3236 on urinary flow and post-void residual volume compared to placebo;
- The effect on progression of LUTS;
- The effect of Org 3236 on sexual function, well-being and LUTS-related Quality of Life compared to placebo;
- The safety of Org 3236;
- The pharmacokinetic (Org 3236) and pharmacodynamic (T, DHT, LH, FSH, E_2, SHBG) properties.

The effects were evaluated during treatment and post-treatment.

Due to a business decision the BPH project was prematurely cancelled and the trial was stopped. Subsequent visits only included safety assessments; efficacy assessments were not analyzed anymore.

Methodology

This was a randomized, double-blind, placebo-controlled, comparative, multi-center, multiple dose trial in subjects with LUTS/BPH.

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Number of subjects (total and for each treatment)

A total of 240 subjects with LUTS/BPH were planned to be enrolled. At the time the trial was stopped, a total of 16 subjects were randomized and on treatment, and an additional nine subjects were only screened.

Diagnosis and criteria for inclusion

1. Signed written informed consent, obtained before screening evaluations;
2. Men diagnosed with LUTS suggestive of BPH:
   - 2.1. Baseline IPSS score of ≥12 (moderate to severe);
   - 2.2. Prostate volume of ≥40 mL and <100 mL (based on TRUS);
   - 2.3. Peak urinary flow rate ≤15 mL/s with a voided volume of ≥125 mL;
3. Age at least 50 but not older than 80 years at screening;
4. PSA <10 ng/mL and exclusion of prostate cancer to the satisfaction of the investigator (e.g., by biopsy).

Test product, dose and mode of administration, batch No.

The test product consisted of tablets containing either 150 µg or 300 µg Org 3236 (etonogestrel). The corresponding batch numbers were [redacted] (150 µg Org 3236) and [redacted] (300 µg Org 3236).
The tablets were administered in doses of 150 µg per two days (in an alternating fashion with placebo), 150 µg per day, or 300 µg per day. The subjects were instructed to take one tablet p.o., per day in the morning, with water.

Duration of treatment

The planned total treatment duration was eight weeks.

Reference therapy, dose and mode of administration, batch No.

Tablets containing placebo with batch number [redacted] For further details see the description of test products (above).

Criteria for evaluation

Due to the early discontinuation of the trial, not all planned evaluations have been performed. Only the actual assessments are presented here.

Efficacy parameters: Prostate volume, the effect on LUTS, urinary flow (Q_{av}), postvoid residual volume, sexual function, well-being and LUTS-related QoL.

Pharmacokinetic-pharmacodynamic parameters: Testosterone.

Safety parameters: (Serious) adverse events ([S]AEs), routine laboratory parameters, PSA, bone markers, physical examination, vital signs and body weight.

Statistical methods

Efficacy: All efficacy data for the AST group including the actual value, change from the baseline, and percentage change from baseline, are presented in a listing by treatment group and visit. No efficacy analysis was performed.

Safety: The safety analysis was performed for the AST group. Adverse events are tabulated and listed per treatment group. Laboratory parameters and vital signs parameters are summarized by treatment group and assessment, and are listed for each subject.

Summary

For a total of 16 treated subjects, the overall mean (SD) age was 67.5 (6.4) years and the mean (SD) BMI was 26.7 (3.6) kg/m^2. All treated subjects were White and of not Hispanic or Latino ethnicity.

The baseline total prostate volumes tended to be higher in the placebo and 300 µg Org 3236 per day groups as compared to the 150 µg Org 3236 per day or per two days groups. For the other demographic and baseline characteristics, no remarkable differences between treatment groups were noted.

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Summary of efficacy

The number of treated subjects was small; therefore no efficacy conclusions can be drawn. An unexpected decrease in total prostate volume was observed in the subjects of the placebo group, which could not be explained. The IPSS total score improved in 11 out of 12 Org 3236 treated subjects, whereas an improvement was observed in only one of the four subjects of the placebo group. Testosterone values rapidly decreased during Org 3236 treatment and returned to baseline values after treatment discontinuation.

Summary of safety

Two to eight weeks treatment with Org 3236 was well tolerated by the 12 treated LUTS/BPH subjects. No SAEs were reported. Two subjects experienced an AE which were considered not to be related to the trial medication. There was no safety concern regarding vital signs, routine laboratory parameters, PSA and bone markers in this small number of subjects.

Conclusions

Due to the early discontinuation of the trial, only 16 subjects were treated for two to eight weeks (12 on Org 3236 and four on placebo treatment). Therefore no efficacy conclusion can be drawn. Org 3236 treatment was well tolerated by this small number of subjects.

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Authorizations

Odin Number: INT00091292

Name	Type	Reason for Signature	Date
[redacted]	Authorized	Authorized	04-Jun-2009 12:20:10