

# Androgen deprivation therapy for volume reduction, lower urinary tract symptom relief and quality of life improvement in patients with prostate cancer: degarelix vs goserelin plus bicalutamide

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## OBJECTIVE

- To assess the efficacy of monthly degarelix treatment for reduction of total prostate volume (TPV), relief of lower urinary tract symptoms (LUTS) and improvement of quality of life (QoL) in patients with prostate cancer (PCa) using monthly goserelin as active control.

## METHODS

- This was a randomized, parallel-arm, active-controlled, open-label, multicentre trial on 182 patients treated with either monthly degarelix (240/80 mg) or goserelin (3.6 mg) for 12 weeks.
- For flare protection, goserelin-treated patients also received daily bicalutamide (50 mg) during the initial 28 days.
- Key trial variables monitored monthly were TPV (primary endpoint), serum testosterone, prostate-specific antigen (PSA), the International Prostate Symptom Score (IPSS) and the Benign Prostate Hyperplasia Impact Index.

## What's known on the subject? and What does the study add?

Androgen deprivation therapy (ADT) is commonly used as a primary treatment for patients with prostate cancer (PCa) who are not eligible for radical treatment options. ADT is also used in patients with PCa as neo-adjuvant hormone therapy to reduce prostate volume and down-stage the disease before radiotherapy with curative intent.

The present study showed that ADT with the gonadotropin hormone-releasing hormone (GhRH) antagonist degarelix is non-inferior to combined treatment with the LHRH agonist goserelin and bicalutamide in terms of reducing prostate volume during the treatment period of 3 months. Degarelix treatment evokes, however, significantly better relief of lower urinary tract symptoms in patients having moderate and severe voiding problems.

## RESULTS

- In all, 175 patients completed the trial (96.1%).
- At week 12, changes in TPV for degarelix and goserelin were similar (–37.2% vs –39.0%) and met the predefined non-inferiority criterion.
- Decreases in IPSS were greater in degarelix than in goserelin-treated patients, differences being statistically significant in patients with baseline IPSS > 13 (–6.7 ± 1.8 vs –4.0 ± 1.0;  $P = 0.02$ ).
- The number of patients with an IPSS change of ≥3 over baseline was also significantly higher in patients treated with degarelix (61.0 vs 44.3%,  $P = 0.02$ ).
- Both treatments were safe and well tolerated.

## CONCLUSIONS

- Medical castration reduces TPV and could also improve LUTS in patients with PCa.
- While the short-term efficacy of degarelix and goserelin + bicalutamide was the same in terms of TPV reduction, degarelix showed superiority in LUTS relief in symptomatic patients, which could highlight the different actions of these drugs on extrapituitary gonadotrophin-releasing hormone (GnRH) receptors in the bladder and/or the prostate.

## KEYWORDS

short-term androgen deprivation, prostate volume reduction, urinary symptom management, patients with prostate cancer

## INTRODUCTION

The hormone-responsive nature of prostate cancer (PCa) means it can be effectively treated with agents that reduce the stimulation of the androgen-sensitive pathways either by blocking the androgen receptor or by decreasing the production of circulating testosterone. Androgen deprivation therapy (ADT) is not only cytostatic but also cytotoxic for hormone-sensitive PCa cells and hence a strong regulator of the survival and growth of the tumour [1]. GnRH agonists remain the most widely used form of ADT. Agonists initially stimulate pituitary GnRH receptors, resulting in a rapid release of gonadotrophins and testosterone (surge), which delays the onset of ADT and has been associated with triggering rare clinical complications such as bladder outlet obstruction and increased pain or spinal cord compression in metastatic patients [2]. To avoid such complications, GnRH agonists in high-risk patients have to be co-administered with an antiandrogen to block effects at testosterone receptor level [3]. By contrast, GnRH antagonist promptly block testosterone production, avoid the testosterone surge and thereby the co-administration of antiandrogens [4]. The efficacy of these two treatment regimes in terms of reducing total prostate volume (TPV) has not been compared systematically.

In almost 70% of patients with PCa, the disease arises from the peripheral zone of the prostate gland, and cause local symptoms (LUTS) only when they have grown to compress or invade proximate structures such as the prostatic urethra, the urinary bladder or the neurovascular bundles [5,6]. Another, more common, reason for the rise of LUTS in patients with PCa is the parallel growth of the prostate due to BPH, which shows increasing prevalence with age [7]. According to Lehrer *et al.* [8], 55.6% of patients with PCa have no to mild symptoms, 37.1% have moderate symptoms, and 7.3% have severe symptoms. There is as yet limited information from randomized clinical trials on the impact of short-term ADT on LUTS and on whether agonist and antagonist GnRH analogues provide similar benefits in this context.

The objective of the present trial was to investigate and compare the effect of 12 weeks of therapy with degarelix 1-month

depot with goserelin acetate 1-month implant, focusing on TPV reduction, LUTS relief and changes of quality of life (QoL) related to urinary symptoms.

## MATERIALS AND METHODS

The present trial was a randomized, parallel-arm, active-controlled, open-label, multicentre trial (Trial identifier at Clinicaltrials.gov is NCT00884273). The inclusion criteria were as follows: age >18 years; histological confirmed PCa (all stages); patients suitable for ADT with a serum PSA level at screening >2 ng/mL; TPV > 30 mL; a bone scan in the past 12 weeks; and an estimated life expectancy of at least 12 months. Protocol-defined exclusion criteria were previously received treatments for PCa, use of a urinary bladder catheter, treatment with a 5- $\alpha$  reductase inhibitor or botulinum toxin in the past 6 months, treatment with alpha-adrenoceptor blocker in the past 4 weeks, or planned radiotherapy during the trial. Patients who received at least one dose of the investigated drug and had at least one efficacy assessment after dosing were included in the full analysis set (FAS). The per-protocol (PP) population was obtained by excluding major protocol violators.

The trial was carried out in compliance with the Helsinki Declaration and the Good Clinical Practice guidelines. Local or regional ethics committees and institutional review boards approved the trial protocol.

Eligible patients were randomized to receive treatment with either monthly degarelix or monthly goserelin for 12 weeks. For patients in the degarelix treatment group, a starting dose of 240 mg (40 mg/mL) degarelix was administered on day 0 as two 3 mL deep injections into the subcutaneous fat of the abdominal wall. The second and third doses (maintenance doses) of 80 mg (at 20 mg/mL concentration) degarelix were administered as single 4 mL s.c. injections on days 28 and 56, respectively. For patients in the control arm, goserelin implants (3.6 mg) were inserted subcutaneously into the abdominal wall every 28th day. On day 0, patients in the goserelin arm were given a 50 mg once-daily oral treatment with bicalutamide for flare protection continuing throughout the first dosing period of 28 days.

Baseline evaluation of the patients included collection of demographic data, medical history, medications, vital signs, electrocardiography, the European Cooperative Oncology Group performance score, and history of PCa, including time since diagnosis, TNM stage and Gleason score. Blood and urine were also collected to establish non-treated baseline values for assessing the changes of key efficacy and safety variables.

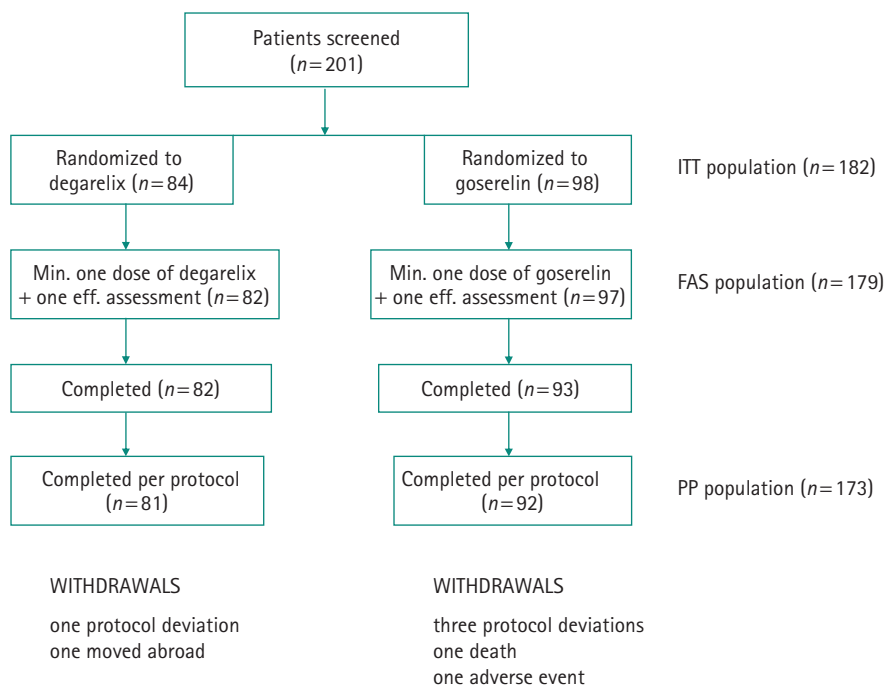
Total prostate volume was measured locally by suitable transrectal ultrasound equipment, the procedure being guided and standardized by a user's manual delivered to each site. The severity of and changes in LUTS during therapy were assessed by the International Prostate Symptom Score (IPSS) questionnaire as used in previous similar studies [9]. Mild LUTS was defined as IPSS of 1–7, moderate LUTS as IPSS of 8–19 and severe as IPSS of 20–35 [10]. Clinical benefits for moderate/severe patients were also assessed for those with a baseline IPSS  $\geq$  13, a commonly used threshold in LUTS trials (e.g. [11]). A clinically meaningful response was defined as an IPSS change of at least three points from baseline [12].

Quality of life related to urinary symptoms was assessed by the separate eighth IPSS question. The patients were asked to score their condition on a scale of 0–6 (delighted, pleased, mostly satisfied, mixed, mostly dissatisfied, unhappy and terrible). Changes of reporting were assessed in three domains: delighted/pleased, mostly satisfied/mixed/ mostly dissatisfied, and unhappy/terrible. The impact of urinary symptoms on various domains of health was also assessed by the Benign Prostate Hyperplasia Impact Index, a self-administered questionnaire [13]. Each of these variables was monitored on a monthly basis.

Blood samples for analyses of testosterone and PSA were collected at each monthly visit before administration of the drug. Testosterone was measured by a validated liquid chromatography system with tandem mass spectrometry assay at Ferring Pharmaceuticals A/S (Copenhagen, Denmark). PSA level was measured by a validated chemiluminescent method at a central laboratory (Esoterix CTS, Hechelen, Belgium).

Safety and tolerability assessments included laboratory values (biochemistry,

FIG. 1. Patient distribution during the course of the clinical trial.



haematology and urine analysis), clinical variables (injection-site tolerability, adverse events [AEs], ECGs, physical examinations, vital signs, and body-weight measurements). A global central laboratory (Esoterix CTS) analysed all clinical chemistry, haematology and urine analysis variables for laboratory safety. The investigator or a medically qualified delegate evaluated the clinical significance of the ECG.

The primary efficacy measure was the mean percentage reduction in TPV from baseline at week 12. In those who had not completed the entire trial, the last observation carried forward (LOCF) approach was used to impute values at week 12. Changes were analysed by analysis of covariance (ANCOVA) using baseline TPV and IPSS score as covariates and treatment arm as factors in the analysis for both the FAS and PP populations. Non-inferiority was considered to be established, if the treatment difference in adjusted mean percentage reduction was significantly greater than  $\Delta = -10$  points in both the FAS and PP analysis sets (two-sided at  $\alpha = 0.05$ ). Changes in IPSS from baseline in the degarelix and goserelin treatment groups (total and selected subgroups) were compared with ANCOVA using treatment arm and country as factors and age and baseline IPSS as covariates.

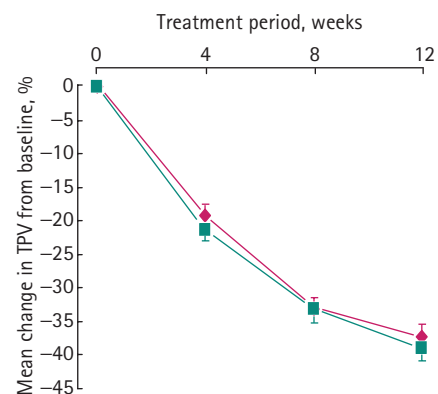
Responder rates in the two treatment groups were compared with Wilcoxon two-sample test. Logistic regression model was established to identify independent predictors of good IPSS response. Changes in QoL due to urinary symptoms were analysed by polytomous regression analysis to each visit. Results are shown as mean  $\pm$  SEM unless otherwise indicated. All analyses were performed and summary statistics calculated using SAS, version 9 or higher.

## RESULTS

Patient disposition throughout the trial is outlined in detail in Fig. 1. Compared with the intended 1:1 randomization, the skewness is due to the fact that randomization was done per site and not per trial basis. Of the 179 patients in the FAS population six had major protocol violation (two had inclusion/exclusion criteria violations and four received prohibited medication before the trial). Accordingly the PP population consisted of 173 patients.

The mean age, weight and BMI of randomized patients were 72.5 years, 79.7 kg and 26.6 kg/m<sup>2</sup>, respectively. All patients were Caucasians. There were no

FIG. 2. Mean ( $\pm$  SEM) percentage change of TPV from baseline during 12 weeks' therapy with either monthly s.c. injections of degarelix (240/80 mg) or monthly s.c. pellets of goserelin (3.6 mg). Patients receiving goserelin treatment also received 50 mg bicalutamide once-daily during the first 4 weeks of the treatment. Red line, degarelix; Green line, goserelin + bicalutamide.



statistically significant differences in the baseline variables between treatment groups (Table 1).

Total prostate volume decreased significantly from baseline to week 12 in both treatment groups with mean percentage decreases of  $-37.2\% \pm 1.8$  and  $-39.0\% \pm 1.8$  for degarelix and goserelin, respectively (Fig. 2). The adjusted difference between treatment groups was 2.4% (95% CI:  $-2.8$ – $7.5\%$ ) for the FAS analysis set and 2.2% (95% CI:  $-3.1$ – $7.6\%$ ) for the PP analysis set. The upper limits of the two-sided 95% CI for the adjusted mean differences were thus below the non-inferiority margin of 10, and therefore non-inferiority was established. The number of patients with a TPV reduction  $<10\%$  after treatment was very low (five patients in each treatment arm).

The median levels of serum testosterone showed no differences between degarelix- and goserelin-treated patients at the scheduled visits. The median level of testosterone for degarelix-treated patients at weeks 4, 8 and 12 was 0.05 ng/mL. The corresponding figures for goserelin were 0.12, 0.05 and 0.05 ng/mL, respectively.

The median percentage changes in PSA level were also similar; for degarelix the decreases from baseline at weeks 4, 8 and 12 were  $-80.6\%$ ,  $-89.7\%$  and  $-92.0\%$ , respectively,

TABLE 1 Baseline characteristics of the trial population. Data are means ± SD or median (range)

Baseline characteristics	Degarelix (N = 82)	Goserelin/bicalutamide (N = 97)	P
Age, years	71.9 (7.71)	73 (7.1)	0.30
Weight, kg	79.7 (12.4)	79.7 (12.2)	0.98
BMI, kg/m <sup>2</sup>	26.8 (4.07)	26.5 (3.72)	0.56
Time since prostate cancer diagnosis, days	89 (217)	102 (270)	0.73
Tumour stage			
Localized	24 (29%)	32 (33%)	0.28
Locally advanced	30 (37%)	23 (24%)	
Metastatic	22 (27%)	31 (32%)	
Not classifiable	6 (7%)	11 (11%)	
T stage			
T1/2	35	42	0.63
T3/4	47	55	
Gleason score			
2–6	17 (21%)	16 (16%)	0.76
7	24 (29%)	31 (32%)	
8–10	41 (50%)	50 (52%)	
ECOG score			
Fully active	52 (63%)	65 (67%)	0.34
Restricted, but ambulatory	28 (34%)	31 (32%)	
Ambulatory, unable to work	2 (2%)	0	
Capable of only limited self-care	0	1 (1%)	
Total prostate volume (mL)	54.8 (26)	49.9 (15.5)	0.14
IPSS	14.3 (6.91)	13.4 (7.36)	0.40
IPSS QoL	2.85 (1.62)	2.73 (1.66)	0.62
BPH Impact Index	5.06 (3.39)	4.58 (3.58)	0.36
PSA level, ng/mL			
Mean	277 (937)	148 (438)	0.25
Median	27.8 (1.9–6206)	15.6 (3–2829)	
Testosterone, ng/mL			
Mean	4.25 (1.88)	4.43 (1.64)	0.48
Median	4.08 (0.32–10.8)	4.33 (0.13–9.61)	

ECOG, European Cooperative Oncology Group.

whilst for goserelin they were –85.2%, –96.6% and –97.3%.

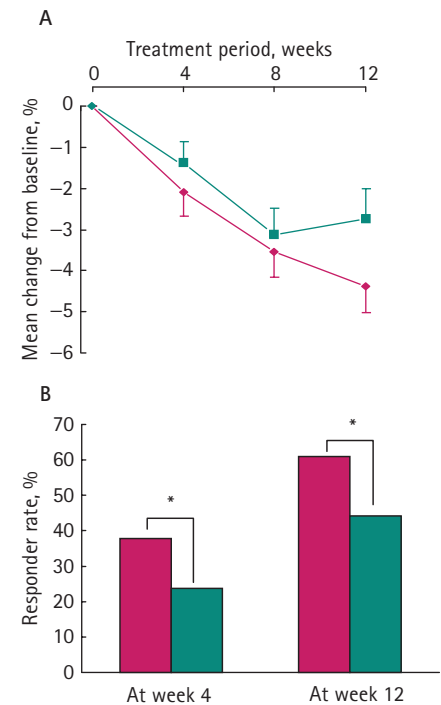
The present trial did not have any specific inclusion criteria regarding IPSS at baseline and hence LUTS varied on a broad scale (22.9% had mild, 62.6% moderate, and 14.5% severe LUTS). Mean total IPSS showed progressive decreases from baseline in both treatment groups (Fig. 3). The mean decreases in degarelix-treated patients (–4.4 ± 0.7) exceeded the three-point threshold for clinical significance, whereas the decreases in the goserelin + bicalutamide group remained below this threshold (–2.7 ± 0.6). The adjusted mean difference between treatment groups, however, did not reach statistical

significance (–1.2, 95% CI: –2.9–0.4; P = 0.15).

Another way of comparing the efficacy of the two medications for LUTS relief was to look at the individual patient's benefit. The percentage of patients showing a clinically meaningful LUTS relief (i.e. IPSS decrease of at least three points) was significantly higher in degarelix- than in goserelin-treated patients at both week 4 (37.8% vs 23.7%, P = 0.04) and week 12 (61.0% vs 44.3%, P = 0.02).

To identify independent predictors of clinically meaningful LUTS relief, we established logistic regression models, including an IPSS change ≥ three points at

FIG. 3. (A) Mean (± SEM) absolute changes in IPSS from baseline during 12 weeks' therapy in patients with PCa with treated degarelix or goserelin + bicalutamide. (B) Percentage of patients with clinically meaningful IPSS response (≥3 points) in the two treatment groups at weeks 4 and 12. Red, degarelix; Green, goserelin + bicalutamide. \*P < 0.05.

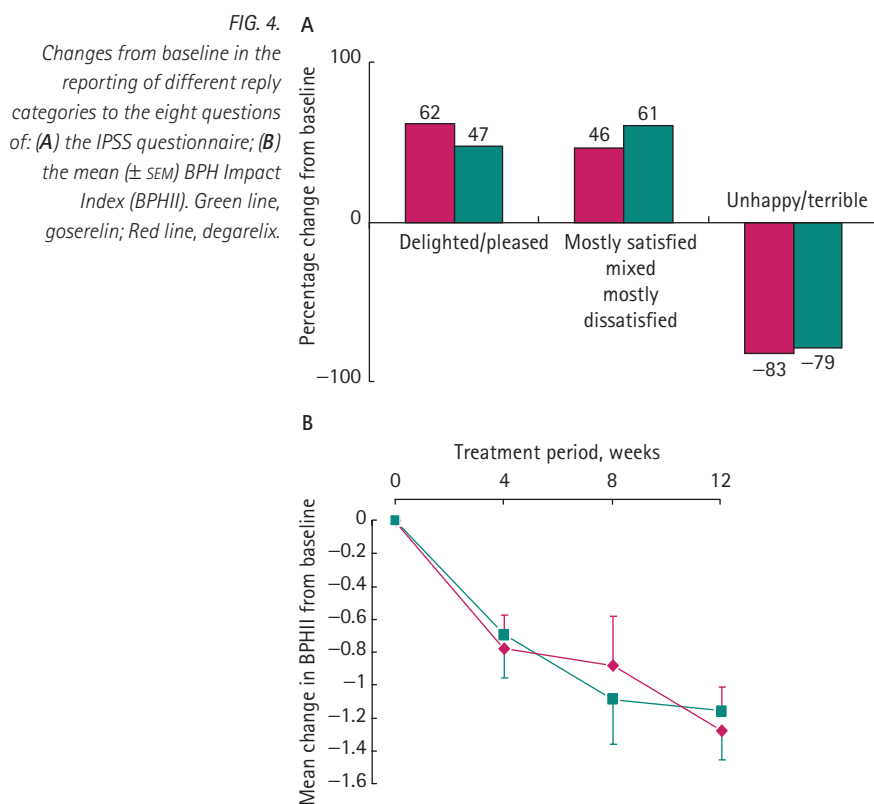


week 4 or 12 as the dependent variable, and age, treatment arm and baseline measures of BMI, testosterone, log PSA, TPV, white blood cell count and Gleason score as independent variables. According to this model, advanced age was associated with decreased probability of clinically meaningful IPSS response (odds ratio [OR] = 0.92, 95% CI: 0.89–0.95, P < 0.001), whereas high BMI (OR = 1.15, 95% CI: 1.06–1.24, P = 0.001) and high log PSA (OR = 1.23, 95% CI: 1.00–1.52, P = 0.05) was associated with increased probability of clinically meaningful IPSS response at week 4. When focusing on the 12-week response, high log PSA at baseline (OR = 1.25, 95% CI: 1.03–1.52, P = 0.02) and degarelix use (OR = 2.09, 95% CI: 1.11–3.96, P = 0.02) were both independently associated with increased probability of achieving clinically meaningful LUTS relief.

In patients with no to mild LUTS only (IPSS 0–7), the magnitude of IPSS changes to

**TABLE 2** Changes in IPSS from baseline in patients treated with degarelix and goserelin + bicalutamide treated stratified according to baseline LUTS severity

LUTS severity at baseline	Degarelix	Goserelin + bicalutamide	P
No to mild LUTS (IPSS 0–7)			
Delta IPSS	-0.81 ± 1.29	-0.40 ± 0.71	0.51
N	16	25	
Moderate LUTS (IPSS 8–19)			
Delta IPSS	-4.52 ± 0.79	-2.10 ± 0.66	0.028
N	54	58	
IPSS ≥ 13			
Delta IPSS	-6.73 ± 0.84	-4.02 ± 0.97	0.023
N	52	55	
Severe LUTS (IPSS 20–35)			
Delta IPSS	-10.80 ± 1.93	-9.57 ± 2.70	0.60
N	12	14	



degarelix or goserelin + bicalutamide were, as expected, clinically insignificant in both arms. By contrast, when focusing on patients who had IPSS 8–19 (moderate) or IPSS ≥ 13 (moderate/severe), mean responses exceeded the three-point threshold for clinical significance and were significantly larger in the degarelix than in the goserelin + bicalutamide group (Table 2).

There was a statistically significant improvement in QoL in terms of urinary symptoms from baseline in both treatment groups ( $P < 0.001$ ). The relative decreases in the reporting of unhappy/terrible from baseline to week 12 were similar in the degarelix and goserelin arms (Fig. 4A). At the end of the trial, there were numerically greater increases in the reporting of 'delighted or pleased' in degarelix-treated

patients than in goserelin-treated patients, whose reporting was more typically 'mostly satisfied/mixed/mostly dissatisfied'. The numerical differences, however, did not reach statistical significance.

The 12-week changes in the Benign Prostate Hyperplasia Impact Index from baseline elicited by both therapies exceeded one point, but showed no major differences between treatment groups (degarelix, -1.28; goserelin, -1.16) (Fig. 4B).

Treatment-emergent AEs were reported by 39% of patients in the degarelix group and 48% of patients in the goserelin group. Most AEs were mild (degarelix group, 31%; goserelin group, 35%) or moderate (degarelix group, 20%; goserelin, 17% group) in intensity with similar distribution between treatment groups. The incidence of severe AEs was greater in the goserelin (11%) than in the degarelix group (2%). In each treatment arm, 35% of patients experienced an AE that was considered possibly/probably related to the drug. Most treatment-emergent adverse drug reactions were injection site reactions (predominantly pain, 14%; erythema, 4%; swelling, 4%), which were reported by degarelix-treated patients only. Other commonly reported reactions were hot flushes (degarelix, 10%; goserelin, 17%), erectile dysfunction (degarelix, 5%; goserelin, 4%) and hyperhidrosis (degarelix, 4%; goserelin, 5%). The incidences of markedly abnormal laboratory or vital sign changes were low and similar between treatment groups (data not shown).

Eight patients reported serious AEs – one in the degarelix and seven in the goserelin group. The one and only serious AE considered possibly related to the drug was ureteric obstruction experienced by a degarelix-treated patient. There was only one serious AE observed in a goserelin-treated patient that led to discontinuation (bladder cancer).

**DISCUSSION**

The main objectives of the present randomized clinical trial were to compare the efficacy of degarelix and goserelin + bicalutamide, focusing on TPV reduction, LUTS relief and related QoL improvement over a 12-week treatment period. The

primary endpoint was successfully met, showing the non-inferiority of degarelix vs goserelin + bicalutamide in terms of reducing TPV in patients with PCa. The magnitude of observed TPV reductions was in the range of what has been reported by similar short-term studies on GnRH agonists (21–54%) [14–19]. This rapid and pronounced TPV reduction could facilitate the more effective delivery of radiotherapy or execution of surgery to patients (neo-adjuvant therapy) but could also provide additional benefits for those complaining of obstructive LUTS at treatment initiation. For comparison, the ≈20% decrease in TPV to degarelix or goserelin + bicalutamide at week 4 is similar to that induced by 5 $\alpha$ -reductase inhibitors – a commonly used medication in patients with BPH with an enlarged prostate (TPV > 30 mL) – over 6–12 months of treatment [20].

Most cancers arise in the periphery of the prostate gland and therefore patients with PCa often remain asymptomatic for quite a long time. However, as the disease progresses and the tumour has grown to compress or invade surrounding structures, such as the prostatic urethra, the bladder or the neurovascular bundles, LUTS could arise [5,6]. Importantly, a significant part of PCa in general practice is discovered when a patient seeks medical help for LUTS, which, however, is often driven by the simultaneously present BPH.

It is well known from the literature that endocrine manipulation can reduce TPV and improve voiding ability in patients with PCa. In 1994 Mommsen *et al.* [21] showed that 62% (43/69) of patients with PCa with acute urinary retention regained their voiding ability within 3 months after surgical castration. Similarly, in a cohort study with 77 patients with PCa, Klarskov *et al.* [22] documented statistically significant changes from baseline in numerous objective measures of voiding when treated with different forms of hormone therapy for 12 months (i.e. 38% increase of  $Q_{max}$  and 15% increase in voiding volume, 36% decrease in postvoid residual volume, 15% decrease in voiding frequency and 67% decrease in symptom score). The bulk of the benefit emerged during the first month of therapy with slow further increases thereafter. On long-term follow-up, the improvements in LUTS persisted during biochemical

progression in most patients, and there was local tumour progression with the need for intervention in only 20% of the patients on Kaplan–Meier estimate after 4 years [23]. As GnRH agonists can improve LUTS in patients with BPH [24], the effect of ADT might also relate to an overall shrinkage of the prostate rather than tumour volume reduction *per se*.

In the present study, the percentage of patients experiencing clinically meaningful LUTS relief was significantly higher in the degarelix than in the goserelin group. Moreover, after eliminating patients with mild symptoms (IPSS 0–7) who were not candidates for medical intervention, degarelix treatment was associated with significantly more pronounced IPSS decreases than goserelin at week 12. Since the differences cannot be ascribed to differences in TPV reduction by the two treatment approaches, seeking alternative explanations seems warranted.

Beyond the indirect effects on testosterone suppression via pituitary receptors, emerging evidence from *in vitro* and *in vivo* animal studies argues that GnRH receptor antagonists might also confer beneficial effects on the static and dynamic components of Bladder Outlet Obstruction via extrapituitary receptors. Indeed, GnRH receptors have been identified on epithelial and smooth muscle cells of the prostate, on peripheral lymphocytes infiltrating the prostate as well as on the bladder mucosa in both animals and in humans [25–30]. GnRH receptor blockade on these cells has been associated with down-regulation of pro-inflammatory cytokines, various growth factors and even  $\alpha$ 1-adrenoreceptors [30,31] with potential implications for smooth muscle relaxation in prostate strips and TPV reduction [30,32]. Moreover, urodynamic (pressure/flow) studies in conscious rats have shown that GnRH antagonists can counteract experimental detrusor overactivity induced by intravesical prostaglandin E<sub>2</sub> [25,29]. The mechanism of action is believed to involve effects on transmitter or cells involved in pathological mechano-afferent activation. Although much remains to be evidenced about the relative contribution of these proposed mechanisms in humans, these experimental findings do seem to support the notion that TPV reduction to ADT is not the only mechanism that can drive symptom relief and that the peripheral effects summarized

herein could possibly explain the more rapid and pronounced relief of LUTS by degarelix than by goserelin in patients with moderate/severe LUTS.

The relief from symptoms was associated with significant QoL improvements from baseline. In line with the trends of IPSS changes, improvements in QoL due to urinary symptoms also tended to favour degarelix-treated patients. On the safety side, both medications were safe and well tolerated with no major differences in overall AE reports. The most common AEs were the typical manifestations of ADT (hot flushes, hyperhidrosis and erectile dysfunction), their incidence rates being in line with what is expected in elderly patients receiving short-term ADT. The only major difference between the two treatments concerned the incidence of injection site reactions, which were only reported by degarelix-treated patients (22% vs 0%), but none of these reactions was severe or constituted a reason to discontinue treatment.

In summary, although the primary goal of ADT – prostate volume reduction – was achieved to the same degree in the two treatment regimes, degarelix had significantly more pronounced effects on LUTS. It seems reasonable to speculate that the observed differences could be due to the difference between the action of an agonist and that of an antagonist on extra-pituitary GnRH receptors in the prostate and/or the urinary bladder [25–30]. Thus, degarelix can be considered as a useful alternative approach to combined GnRH agonist plus antiandrogen therapy for patients with PCa who are in need of short-term neo-adjuvant ADT. The clinical benefit of degarelix in terms of providing clinically meaningful LUTS relief warrants further exploration in future urodynamic (pressure-flow) investigations.

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#### CONFLICT OF INTEREST

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- Abbreviations:** ADT, androgen deprivation therapy; AEs, adverse events; ANCOVA, analysis of covariance; FAS, full analysis set; IPSS, International Prostate Symptom Score; PCa, prostate cancer; PP, per protocol; QoL, quality of life; TPV, total prostate volume.