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Comparison of the Impact of Degarelix and Leuprolide on the Health-Related Quality of Life of Patients with Prostate Cancer: Results of a 12-Month Phase III Clinical Trial

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ABSTRACT

Introduction: The objective of this study was to compare health-related quality of life (HRQoL) with degarelix (240 mg in month 1 and then 80 mg monthly, administered subcutaneously) or leuprolide (7.5 mg/month intramuscularly) in men with prostate cancer.

Methods: HRQoL was assessed at baseline and throughout a 12-month randomized, open-label, parallel-group clinical trial using standard SF-12 and EORTC QLQ-C30 questionnaires. HRQoL outcomes were compared between treatments using trend, change score, and response analyses.

Results: HRQoL data from 401 subjects were included in this analysis; 205 receiving degarelix 240/80 mg and 196 receiving leuprolide 7.5 mg. Over the 12-month treatment period, patients experienced worsening of most HRQoL domains except for bodily pain, general health (both SF-12), and diarrhea (QLQ-C30). No treatment group differences in HRQoL were noted at day 28 or 6 months. At 12 months, mean SF-12 scores for the mental component summary ($p = 0.02$) and mental health ($p = 0.04$) were significantly higher in degarelix- compared with leuprolide-treated patients. Treatment with leuprolide had a seemingly more favorable impact on insomnia (QLQ-C30; $p = 0.04$) and bodily pain (SF-12; $p = 0.006$) compared with degarelix. Patients with metastatic disease treated with degarelix reported significant improvements in the role-emotional domain (SF-12; $p = 0.02$), global health status (QLQ-C30; $p = 0.04$), and appetite loss (QLQ-C30; $p = 0.02$) at 12 months compared with leuprolide.

Conclusions: After 12 months of treatment, the HRQoL of patients with advanced prostate cancer treated with the GnRH antagonist degarelix is similar to that of patients treated with leuprolide. The study also indicates benefits with degarelix treatment in the metastatic population.

KEYWORDS: Degarelix; Gonadotropin-releasing hormone agonist; Gonadotropin-releasing hormone antagonist; Health-related quality of life; Leuprolide; Prostate

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INTRODUCTION

Prostate cancer and its treatments often have a substantial impact on a patient's health-related quality of life (HRQoL). Multiple HRQoL components may be affected, including sexual dysfunction, lower urinary-tract dysfunction, bowel changes, bone pain, fatigue, sarcopenia, and anemia [1, 2].

Maintenance or improvement of HRQoL is increasingly recognized as a key goal of therapy in prostate cancer and is an important issue when considering the various hormonal treatment options. In fact, the primary treatment goal for patients with advanced or metastatic prostate cancer is often to sustain HRQoL [3]. Since therapies with different mechanisms of action may have different and specific effects on HRQoL, relative benefits may contribute to better compliance and thereby overall efficacy of the treatment [4].

Clinical trials assessing HRQoL in patients with localized or advanced prostate cancer have shown inconsistent results. Generally, active treatment options tend to negatively affect patients' HRQoL [5, 6]. Conflicting results are evident from trials of complete androgen blockades with flutamide in surgically castrated men with prostate cancer. Specifically, emotional functioning worsened as early as 3 months post treatment while overall HRQoL improved (as assessed by the Short Form-36 and the UCLA Prostate Cancer Index) during the first 12 months of treatment [6, 7]. Similarly, a clinical trial comparing various androgen-deprivation therapy (ADT) regimens (i.e., leuprolide, goserelin, or cyproterone) with close monitoring of age-comparable healthy volunteers found, among ADT patients, significant improvements in physical/urinary function but clinically significant deterioration in sexual, social/role, and subjective cognitive functions [8].

The gonadotropin-releasing hormone (GnRH) blocker (or antagonist), degarelix, directly blocks GnRH receptors. It produces a rapid reduction in serum testosterone levels without inducing the clinical "flare" and the associated potential for detrimental effects observed with GnRH agonists [9]. Moreover, the faster onset of effect with GnRH antagonists may offer increased efficacy, enhanced apoptotic effect, faster tumor volume reduction, and quicker relief from cancer symptoms [10, 11]. Thus, differences between these 2 agents may be anticipated in the context of quality of life measures. Given the importance of HRQoL to patients and its role in treatment decisions, HRQoL data from the degarelix and leuprolide Phase III randomized trial among males with advanced prostate cancer [12] were analyzed. For simplification, and given the similar results for both degarelix doses, this paper focuses only on the degarelix 240/80 mg (marketed dose) and leuprolide treatment groups.

METHODS

Patients and Treatment

This study analyzed HRQoL parameters in a 12-month randomized, active-controlled, open-label, parallel-group Phase III trial among patients with advanced prostate cancer (NCT00295750) [12]. The intent-to-treat population consisted of 610 men (degarelix 240/160 mg, n = 202; degarelix 240/80 mg, n = 207; Leupron Depot [leuprolide] 7.5 mg, n = 201) aged $\geq$18 years with histologically confirmed adenocarcinoma of the prostate. Patients were included in the study if they had biochemical failure and hormone-sensitive disease, serum testosterone levels of >1.5 ng/mL, Eastern Cooperative Oncology Group scores of $\leq$2, and PSA levels of $\geq$2 ng/mL. Patients were excluded if they were candidates for curative therapy. The primary endpoint of the trial was suppression of testosterone to $\leq$0.5 ng/mL between 28 days and 12 months, and a secondary endpoint was HRQoL [12, 15]. The trial was conducted in Europe and North America among patients with all prostate cancer stages and Gleason grades of cancer.

Patients were randomized to 1 of 3 treatment groups. Patients in the degarelix treatment groups received a starting dose of 240 mg at a concentration of 40 mg/mL, followed by 12 additional single doses of either 80 mg at a concentration of 20 mg/mL or 160 mg at a concentration of 40 mg/mL every 28 days. Patients in the leuprolide group received a 7.5 mg depot every 28 days. In the leuprolide group, bicalutamide 50 mg daily could be given at the start of treatment for flare protection at the discretion of the investigator.

Assessment of HRQoL

HRQoL data were collected at baseline and on days 1, 28, 84, 168 (6 months), and 12 months. Two self-administered HRQoL instruments were used: version 2 of the Short Form-12 (SF-12 v2) and the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30).

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The SF-12 is a brief (12 item), reliable, validated measure of health status, covering 8 domains relating either to physical or mental HRQoL, with a score range from 0 to 100 [13-15]. SF-12 scale scores were standardized for a US population and norm-based for a mean score of 50 and a standard deviation of 10 [13]. For all scales, higher scores denote better functioning. Results are presented by each of the 8 domains and summarized into 2 scores: a physical component summary (PCS) and mental component summary (MCS). The PCS includes the physical functioning, role physical, bodily pain, and general health domains. The MCS consists of the vitality, social functioning, role emotional, and mental health domains. Cross-validation of the SF-12 in 9 European countries (Denmark, France, Germany, Italy, Norway, the Netherlands, Spain, Sweden, and the United Kingdom) has shown a high degree of correspondence on summary scores, allowing for valid large-group comparisons of overall physical and mental health outcomes within this multi-national study [14].

The EORTC QLQ-C30 has also been validated in 81 languages and has been commonly used in prostate cancer trials [16]. The instrument measures global health status and a variety of functional domains, including physical, role emotional, cognitive, and social functioning, as well as various symptoms, including fatigue, nausea and vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties. All scale scores range from 0 to 100. High scores on the global health status and functioning scales indicate better quality of life, while high scores on the symptom scales suggest worsening conditions, and thus poorer quality of life.

Statistical Analysis

To compare the 2 treatment arms, degarelix 240/80 mg and leuprolide, the following analyses were conducted: (1) trend (over time); (2) change score (baseline versus end of study); and (3) responder (percentage of patients classified as "better," "same," or "worse" from baseline to end of study). Fewer than 20% of patients at each visit had missing HRQoL data. In cases of missing data, calculations were conducted using the last-observation-carried-forward (LOCF) method.

Trend analyses were done by analysis of covariance that controlled for baseline HRQoL scores across all assessment time points. These were done overall and by baseline-assessed cancer stage (localized, locally advanced, and metastatic). To assess treatment group mean differences, T-tests were applied: at day 28, 6 months, and 12 months for trend analyses, and from baseline to 12 months for change scores. For responder analyses, the criteria for improvement ("better") or decline ("worse") was based on minimal important differences (MID), calculated using the 0.5 standard deviation (SD) approach, a threshold well-accepted in clinical studies [17]. The 0.5 SD approach is standardized at a 5-point change for PCS and MCS. A 0.5 SD threshold for MID was also applied to the baseline score distribution of SF-12 and EORTC QLQ-C30 domains. Chi-square statistics were used to compare the proportion of patients within each treatment group scoring "better" on any given HRQoL scale.

All analyses utilized a p-value of $p < 0.05$ for statistical significance. For change-score analyses, effect sizes (ES) were computed to access the magnitude of treatment benefit within and between groups. The ES were compared using Cohen's suggested criteria: ES of 0.2 or 0.3 suggest a small effect; 0.5, a medium effect; and 0.8 and greater, a large effect [18]. Due to the exploratory nature of the analysis, a multiple-comparisons correction was not applied to the data.

RESULTS

HRQoL data at the baseline were analyzed for 401 subjects (degarelix 240/80 mg: n = 205; leuprolide 7.5 mg: n = 196). Most patients were white (84%) and the mean patient age was 72 years. No significant differences were observed between treatment groups for baseline demographic and clinical characteristics (Table 1).

Significant differences between treatment groups at baseline were observed for the following sub-scores on the EORTC QLQ-C30: the role functioning, emotional functioning, social functioning domains, and insomnia and diarrhea. Baseline SF-12 and EORTC QLQ-C30 scores are shown in Table 2.

Trend Analyses

Trend analyses over the 12 months showed a minor though statistically significant worsening in function and symptoms in both treatment groups for all HRQoL scales (all $p < 0.05$) except for the following, which showed no change: bodily pain and general health on the SF-12, and diarrhea on the EORTC QLQ-C30. In no case was the change in HRQoL scale

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Table 1. Baseline patient demographic and clinical characteristics.

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Variable	Description	Degarelix (n = 205)	Leuprolide (n = 196)
Age (years)	Mean (SD)	71.6 (8.16)	72.3 (8.77)
	Median (min, max)	72 (51, 89)	74 (52, 98)
Race (%)	White	170 (82.9)	167 (85.2)
	Hispanic	25 (12.2)	21 (10.7)
	American Indian/Alaskan	18 (8.8)	19 (9.7)
	Black/African heritage	16 (7.8)	10 (5.1)
	Asian	1 (0.5)	0 (0.0)
Region (%)	Europe	120 (58.5)	115 (58.7)
	USA	47 (22.9)	41 (20.9)
	Canada	22 (10.7)	22 (11.2)
	Mexico	16 (7.8)	18 (9.2)
Time since diagnosis (years)	Mean (SD)	1.1 (2.64)	1.0 (2.87)
	Median (min, max)	0 (0, 14.0)	0 (0, 18.0)
Cancer stage (%)	Localized	68 (33.2)	62 (31.6)
	Locally advanced	63 (30.7)	52 (26.5)
	Metastic	37 (18.0)	46 (23.5)
	Not classifiable	37 (18.0)	36 (18.4)
Gleason score (%)	2-4	20 (9.8)	24 (12.3)
	5-6	67 (32.7)	59 (30.3)
	7	63 (30.7)	61 (31.3)
	8-10	55 (26.8)	51 (26.2)

SD = Standard deviation

score considered to be of clinical significance. The change in symptom scale of nausea/vomiting on the EORTC QLQ-C30 neared statistical significance (p = 0.056), trending toward increases in this symptom. At 12 months, a significant difference was observed between degarelix and leuprolide on MCS (p = 0.027) and its component, mental health (p = 0.046), showing less decline in function for patients who received degarelix. No other significant differences between treatment arms at 12 months were found and none were observed at 28 days on either the SF-12 or EORTC QLQ-C30. Table 3 shows trend analysis results for each treatment group at day 28, 6 months, and 12 months.

Change Scores

No significant treatment group differences were observed on change scores from the SF-12 or EORTC QLQ-C30 scales, except for insomnia (EORTC QLQ-C30) where patients who received leuprolide showed less of an increase in this symptom (ES = 0.26, p = 0.04, leuprolide: mean change = 5.19, SD = 30.02; degarelix: mean change = 7.29, SD = 26.76) from baseline. No other treatment group change score differences produced an ES of "small" or greater.

Responder Analyses

For responder analyses, compared with degarelix (16.4%), a significantly greater proportion of patients receiving leuprolide (30.1%) improved on bodily pain (SF-12, p = 0.006; Chi-square = 10.28). No other treatment-group responder percent differences were significant. The percentage of patients with a "better" domain score with degarelix 240/80 mg or leuprolide at the end of the study versus baseline is shown for all domains in Table 4.

Trend Analyses by Cancer Stage

At day 28, patients with localized cancer showed significant worsening in general health (SF-12; p = 0.026), role emotional (SF-12; p = 0.003), and fatigue (EORTC QLQ-C30; p = 0.037) with degarelix compared with leuprolide. In contrast, locally advanced patients receiving degarelix scored better on MCS (SF-12; p = 0.048) and vitality (SF-12; p = 0.042) at 28 days. No other differences were observed between treatment groups by cancer stage at 28 days or 6 months.

At 12 months, no significant differences were observed between treatment groups among patients with localized or locally advanced disease. Among patients with metastatic disease at 12 months, improvements were noted for role emotional (SF-12; p = 0.028), global health status (EORTC QLQ-C30; p =

Table 2. SF-12 and EORTC QLQ-C30 mean scores at baseline.
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	Degarelix (n = 188)		Leuprolide (n = 179)	
	Mean	SD	Mean	SD
SF-12				
Composite scales				
PCS	46	9	45	10
MCS	51	9	49	10
Physical QOL scales				
Physical function	46	10	46	11
Bodily pain	50	10	48	10
Role physical	46	10	44	9
General health	43	11	43	11
Mental QOL scales				
Vitality	53	11	53	11
Social functioning	47	11	46	12
Role emotional	46	10	44	11
Mental health	52	10	51	10
EORTC QLQ-C30				
Functional scales				
Global health status	67	18	67	20
Physical functioning	82	18	82	18
Role functioning*	85	20	80	24
Emotional functioning*	84	16	80	18
Cognitive functioning	85	15	83	18
Social functioning*	88	17	84	21
Symptom scales				
Fatigue	23	19	27	20
Nausea and vomiting	4	9	3	8
Pain	17	21	20	24
Dyspnea	11	20	11	21
Insomnia*	16	23	24	27
Appetite loss	11	21	10	19
Constipation	16	26	14	25
Diarrhea*	4	11	7	14
Financial difficulties	14	22	17	26

MCS = mental component summary; PCS = physical component summary; SD = standard deviation
Data rounded to the nearest whole number.
*p <0.05 degarelix versus leuprolide.

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Figure 1. HRQoL: patients with metastatic disease: a) Role emotional; b) Global health status/QoL; c) Appetite loss.*
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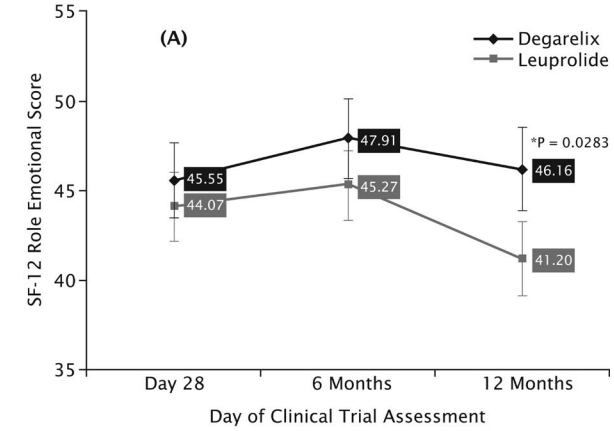
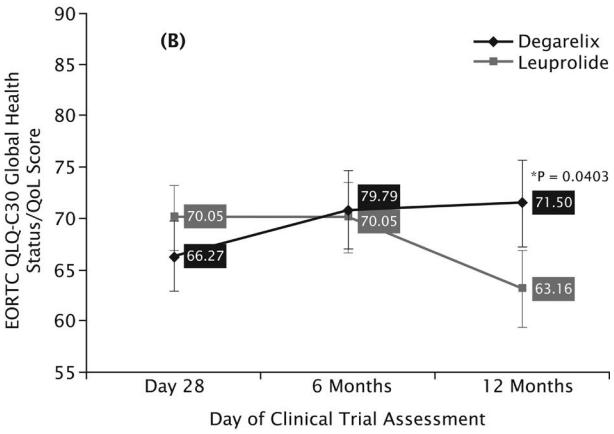
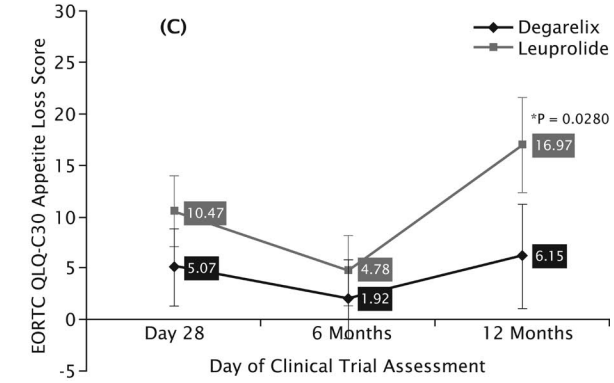
Note: Estimated least square means are presented, using baseline as a covariate. 95% confidence intervals are shown surrounding each mean (based on 83.4%, yielding a probability of overlap of 0.95, see Schenker et al. [20]). * Statistically significant differences are noted for degarelix compared to leuprolide.







0.04), and appetite loss (EORTC QLQ-C30; p = 0.028) for the degarelix group compared with leuprolide (Figure 1).

DISCUSSION

Due to poor prognoses and disease outcomes associated with advanced prostate cancer, treatment decisions may be in part based on a therapy's impact on patient HRQoL. The HRQoL differences between ADT options may affect treatment decisions not only for patients with metastatic disease receiving ADT as palliative therapy but also for patients with less-advanced disease. Hormonal therapy is increasingly used in men with earlier disease (i.e., non-metastatic) or recurrent disease after definitive treatment. Many patients for whom long-term ADT is indicated are still young and physically and sexually active, and so HRQoL is an issue of paramount importance when considering the various hormonal treatment options in these patients. The current study suggests that, after 12 months of treatment, the HRQoL of patients with advanced prostate cancer treated with degarelix, a GnRH antagonist, is comparable with that for patients treated with leuprolide. Although trend analyses over 12 months showed a worsening in function and symptoms in both treatment groups, no clinically significant changes in HRQoL were observed. However, some specific HRQoL issues may favor the selection of 1 or other of these agents, and so consideration of these aspects should inform final treatment decisions.

Degarelix has been shown to be as effective as leuprolide in suppressing testosterone from day 28 to day 364 [12]. Current study results suggest that degarelix and leuprolide may also have a similar impact on physical aspects of HRQoL. However, the deterioration in mental aspects of quality of life may be less with degarelix. While declines in most function areas were observed for all patients across the 12-month trial, patients treated with degarelix 240/80 mg showed less deficit in mental quality of life (MCS and mental health on the SF-12) than those treated with leuprolide at 12 months. One possible explanation for this difference could be different modes of action of the agonist and the antagonist at the pituitary/hypothalamic level. Thus, GnRH agonists produce an initial stimulation of GnRH receptors, which result in increased luteinizing hormone, follicle-stimulating hormone, and testosterone secretion. The sustained pituitary overstimulation gradually down-regulates/desensitizes GnRH receptors, producing a decrease in hormone levels [19]. Conversely, GnRH antagonists block GnRH receptors,

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Table 3. SF-12 and EORTC QLQ-C30 least squared mean scores: day 28, 6 months, and 12 months.

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	Day 28				6 Months				12 months			
	Degarelix (n = 199)		Leuprolide (n = 192)[a]		Degarelix (n = 201)		Leuprolide (n = 192)[a]		Degarelix (n = 200)		Leuprolide (n = 187)[b]	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE
SF-12												
Composite Scales												
PCS	45	0	45	0	44	1	45	1	44	1	44	1
MCS	51	1	51	1	51	1	50	1	50*	1	48	1
Physical QOL scales												
Physical function	45	1	46	1	44	1	45	1	44	1	44	1
Bodily pain	50	1	49	1	48	1	49	1	48	1	48	1
Role physical	46	1	46	1	44	1	46	1	44	1	44	1
General health	44	1	44	1	44	1	43	1	44	1	43	1
Mental QOL scales												
Vitality	54	1	54	1	53	1	53	1	53	1	51	1
Social functioning	47	1	47	1	47	1	48	1	47	1	46	1
Role emotional	45	1	46	1	44	1	45	1	44	1	43	1
Mental health	53	1	53	1	53	1	52	1	52†	1	50	1
EORTC QLQ-C30												
Functional scales												
Global health status	68	1	70	1	67	1	69	1	68	1	66	1
Physical functioning	82	1	83	1	82	1	83	1	80	1	80	1
Role functioning	83	1	86	1	83	1	85	1	81	2	80	2
Emotional functioning	85	1	84	1	84	1	83	1	82	1	81	1
Cognitive functioning	84	1	86	1	84	1	84	1	82	1	81	1
Social functioning	86	1	89	1	89	1	89	1	85	1	85	2
Symptom Scales												
Fatigue	24	1	22	1	25	1	25	1	27	2	26	2
Nausea and vomiting	2	1	4	1	2	1	3	1	3	1	4	1
Pain	14	1	16	1	15	1	16	1	17	2	18	2
Dyspnea	14	1	13	1	13	1	15	1	17	1	18	1
Insomnia	22	2	19	2	25	2	21	2	26	2	23	2
Appetite loss	7	1	9	1	7	1	7	1	9	2	12	2
Constipation	14	1	13	1	14	1	13	2	17	2	15	2
Diarrhea	4	1	5	1	4	1	3	1	5	1	4	1
Financial difficulties	11	1	12	2	9	1	10	1	9	1	10	2

MCS = mental component summary; PCS = physical component summary; SE = standard error; QOL = quality of life

Data rounded to the nearest whole number.

*p = 0.027 and †p = 0.046 for degarelix versus leuprolide; Patient numbers for leuprolide varied for the EORTC QLQ-C30: [a]N = 190; [b]N = 185

which results in a rapid testosterone suppression without an initial luteinizing hormone and testosterone surge.

While physical and global HRQoL scores (e.g., PCS, general health, global-health status) were comparable between the treatment groups at 12 months, the end-of-study change score and responder analyses suggest that patients receiving degarelix may have experienced more bodily pain and insomnia than their leuprolide counterparts. However, the mean increase in insomnia seen in the degarelix group during the study may be explained in part by the significantly lower levels of insomnia reported at the baseline among this group.

The impact of therapy on HRQoL is especially important among patients with metastatic prostate cancer for whom treatment is primarily palliative [4, 7]. When patients were analyzed by cancer stage subgroups, a positive impact of degarelix was observed among patients with metastatic disease at 12 months. Specifically, patients who received degarelix scored better than those who received leuprolide on global health status (EORTC QLQ-C30), role emotional (SF-12), and appetite loss (EORTC QLQ-C30). While degarelix may have an overall positive impact on patient mental HRQoL compared with leuprolide at 12 months, cancer stage results suggest that this impact may be broader, incorporating global HRQoL improvement among patients with metastatic disease.

During this pivotal Phase III trial, degarelix was shown to induce a rapid reduction in testosterone to castrate levels, observed within 3 days in the majority of patients [12]. However, in the leuprolide arm, castrate levels were not observed until 28 days after starting treatment, and for some patients only after they had experienced a testosterone surge. However, it is difficult to predict the HRQoL effect of a fast onset of action. While some patients will suffer from the unpleasant consequences of a rapid fall in testosterone, others will benefit from a rapid reduction in metastatic pain and the knowledge that the cancer is being treated following an initiation of therapy with no delay. Indeed, the HRQoL data show a rather unclear and complicated picture. No overall treatment group differences or differences by cancer stage were observed at day 28. However, at day 28, patients with localized cancer, receiving degarelix, showed significant worsening compared with leuprolide in several domains of the SF-12 and in fatigue in the EORTC QLQ-C30, possibly due to the sudden change in testosterone.

Table 4. Responder analyses: Proportion of patients with "better" domain score at end of study versus baseline.
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	% patients "better" at end of study versus baseline	
Domain	**Degarelix 240/80 mg**	**Leuprolide**
SF-12		
Composite scales		
PCS	19	25
MCS	30	22
Physical QOL scales		
Physical function	20	17
Bodily pain	16	30*
Role physical	16	21
General health	27	24
Mental QOL scales		
Vitality	26	21
Social functioning	24	24
Role emotional	29	28
Mental health	35	29
EORTC QLQ-C30		
Functional scales		
Global health status	27	25
Physical functioning	18	18
Role functioning	20	25
Emotional functioning	17	22
Cognitive functioning	22	23
Social functioning	19	28
Symptom scales		
Fatigue	31	33
Nausea and vomiting	11	10
Pain	28	35
Dyspnea	7	8
Insomnia	14	22
Appetite loss	15	12
Constipation	17	19
Diarrhea	8	13
Financial difficulties	21	24

*Bodily pain better for leuprolide

But patients with locally advanced disease, who were receiving degarelix, showed improvement on MCS and vitality.

As potential limitations to the interpretation of the findings, some methodological considerations should be pointed out. The LOCF method was used to compensate for missing data due to patient discontinuation, unrecorded patient visits, and incomplete HRQoL assessments at study visits. Although sensitivity analyses were conducted with observed data and these yielded similar results as those conducted among the LOCF dataset, missing patient-visit data may have affected study findings. Further, pooled study results represented a multi-national patient population, limited in sample size for regional analysis. The rather unclear and complicated picture shown by the HRQoL data may be related to the lack of a more sensitive, disease-specific HRQoL instrument. Although the HRQoL instruments used in this study are highly validated, some variability in HRQoL outcomes was observed. This may, in part, be a consequence of the subjective nature of these areas of measurement. In addition, the study protocol allowed bicalutamide to be administered at the physician's discretion at the start of treatment to protect against clinical flare in leuprolide patients. Since the addition of bicalutamide-to-patient treatment regimens was neither regulated nor randomized, the clinical impact of its use and the potential confounding effect on the HRQoL comparison of degarelix and leuprolide was not assessed.

CONCLUSION

Degarelix, a GnRH antagonist, has been shown to induce a rapid and profound testosterone response in patients with advanced prostate cancer. This study was the first to present the treatment impact of degarelix, compared with leuprolide, on prostate cancer HRQoL, contributing to the body of literature informing physicians and patients confronted with prostate-cancer treatment choices. This study suggests that the impact on HRQoL of degarelix and leuprolide was largely comparable. However, differences were observed in MCS and mental health, both favoring degarelix at 12 months, and in insomnia (change score) and bodily pain (responder analysis) favoring leuprolide. Apparent benefits in HRQoL (role emotional domain, global health status, and appetite loss at 12 months) were also observed with degarelix treatment versus leuprolide in the metastatic population. The rapid onset of testosterone suppression achieved with degarelix may be important for prostate cancer management and may be of particular benefit in symptomatic patients with advanced/metastatic disease. Further studies are needed to confirm these preliminary observations. In an era of personalized medicine, knowledge of apparent differences between treatments in terms of their impact on various domains of HRQoL may offer another dimension to clinical decision-making with regard to a selection of agents for ADT in individual patients with prostate cancer.

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APPENDIX

The following centers participated in this study:

Canada: Brantford Urology Research, Brantford, Ontario; Bruce W. Palmer Urology Inc., Kentville, Nova Scotia; Burlington Professional Centre, Burlington, Ontario; Can-Med Clinical Research Inc., Victoria, British Columbia; Dr. Cal Andreou Research, Surrey, British Columbia; Dr. Gary Steinhoff Clinical Research, Victoria, British Columbia; Mor Urology, Inc., Newmarket, Ontario; Quest Clinical Trials, Markham, Ontario; The Female/Male Health Centres, Oakville, Ontario; The Male Health Center, Toronto, Ontario; The Male and Females Health and Research Centres, Barrie, Ontario; The Urology Resource Centre, Burlington, Ontario; Urology South Shore Research, Greenfield Park, Quebec. **Czech Republic**: Fakultni Nemocnice Olomouc, Olomouc; Fakultni Nemocnice v Motole, Prague; Nemocnice Jindrichuv Hradec, a.s., Jindrichuv Hradec; Slezska Nemocnice, Opava; Urocentrum Brno, Brno; Vseobecna Fakultni Nemocnice v Praze, Prague. **Germany**: Klinikum der Universität Regensburg, Regensburg; Urologische Klinik Universitatsklinikum Mannheim, Mannheim. **Hungary**: B.A.Z. Megyei Korhaz-Rendelointezet, Miskolc; Fovarosi Onkormanyzat Uzsoki utcai Korhaza, Budapest; Miskolc MJV Semmelweis Korhaz, Miskolc; Pecsi Tudomanyegyetem AOK, Pecs; Petz Aladar Megyei Korhaz, Gyor; Szeged M. J. V. O. Korhaza, Szeged; Szent Lukacs Egeszsegugyi Kht. Dombovar. **Mexico**: Centro Medico Dalinde, Mexico City; Consultorio Medico, Zapopan, Jalisco; Hospital Aranda de la Parra, Leon; Hospital Christus Muguerza del Parque, Chihuahua; Hospital Dr. Angel Leaño, Zapopan, Jalisco; Hospital General "Dr. Santiago Ramon

y Cajal," Durango; Hospital Santa Fe, Mexico City; Instituto Mexicano de Transplantes, Cuernavaca; Instituto Nacional de Ciencias Medicas y Nutricion "Salvador Zubiran," Mexico City; Instituto Estatal de Cancerologia "Dr. Arturo Beltran Ortega," Acapulco. **The Netherlands**: Atrium MC, Heerlen; Catharina-ziekenhuis, Eindhoven; Ziekenhuis Gelderse Vallei, Ede. **Romania**: "C.I. Parhon" Clinical Hospital, Iasi; "Fundeni" Clinical Institute, Bucharest; Mures Clinical County Hospital, Tg. Mures; Private Medical Center, Arad; Prof. Dr. Th. Burghele Hospital Bucharest, Bucharest; Provita Center, Constanta; Sibiu County Clinical Hospital, Sibiu; St John Clinical Emergency Hospital, Bucharest. **Russia**: Andros Urology Clinic, St. Petersburg; City Clinical Hospital #1 named after N.I.Pirogov, Moscow; Moscow State Medico-Somtological University, Moscow; Municipal Clinical Hospital 60#; Moscow; Municipal Multi-Speciality Hospital #2, St. Petersburg; St. Petersburg Mechnikov State Medical Academy, St. Petersburg. **Ukraine**: Dniepropetrovsk State Medical Academy, Dnipropetrovsk; Kharkov Reg. Clin. Centre of Urology & Nephrology, Kharkov; Kiev City clinical Hospital # 3, Kiev; Odessa State Medical University, Odessa. **United Kingdom**: Clatterbridge Centre For Oncology, The Wirral; Derriford Hospital, Plymouth. **USA**: Advanced Urology Medical Center, Anaheim, CA; Alaska Clinical Research Center, Anchorage, AK; Alliance Urology Specialists, Greensboro, NC; Florida Foundation For Healthcare Research, Ocala, FL; Grand Strand Urology, Myrtle Beach, SC; Hospital Andres Grillasca, Puerto Rico; Lawrenceville Urology, Lawrenceville, NJ; North Urology Research, Concord, NC; Office of Jay A. Motola, MD, Carmel, NY; Regional Urology, Shreveport, LA; Renstar Medical Research, Ocala, FL; Seattle Urology Research Center, Seattle, WA; South Florida Medical Research, Aventura, FL; South Orange County Medical Research Center, Laguna Hills, CA; State College Urologic Association, State College, PA; University of Colorado Health Sciences Center, Aurora, CO; Urology Associates Research, Denver, CO; Urology Centers Of Alabama, Homewood, AL; Urology San Antonio Research, San Antonio, TX; Urology of Virginia, Norfolk, VA; Western Clinical Research, Torrance, CA.

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