

## Original Article

# Efficacy and safety of a 3-month dosing regimen of degarelix in Japanese patients with prostate cancer: a phase II maintenance-dose-finding study

Seiichiro Ozono<sup>1,\*</sup>, Taiji Tsukamoto<sup>2</sup>, Seiji Naito<sup>3</sup>, Yasuo Ohashi<sup>4</sup>, Takeshi Ueda<sup>5</sup>, Tsutomu Nishiyama<sup>6</sup>, Hideki Maeda<sup>7</sup>, Hidehito Kusuoka<sup>8</sup>, Rio Akazawa<sup>9</sup>, Mototsugu Ito<sup>10</sup>, and Hideyuki Akaza<sup>11</sup>

<sup>1</sup>Department of Urology, Hamamatsu University School of Medicine, Shizuoka, <sup>2</sup>Department of Urology, Sapporo Medical University, Hokkaido, <sup>3</sup>Department of Urology, Harasanshin Hospital, Fukuoka, <sup>4</sup>Department of Integrated Science and Engineering for Sustainable Society, Chuo University, Tokyo, <sup>5</sup>Prostate Center and Division of Urology, Chiba Cancer Center, Chiba, <sup>6</sup>Department of Urology, Uonuma Institute of Community Medicine, Niigata University Medical and Dental Hospital, Niigata, <sup>7</sup>Medical Research, Medical Affairs, Astellas Pharma Inc., Tokyo, <sup>8</sup>Japan-Asia Clinical Development 1, Development, Astellas Pharma Inc., Tokyo, <sup>9</sup>Japan-Asia Data Science, Development, Astellas Pharma Inc., Tokyo, <sup>10</sup>Japan-Asia Clinical Pharmacology, Development, Astellas Pharma Inc., Tokyo, and <sup>11</sup>Strategic Investigation on Comprehensive Cancer Network, The University of Tokyo, Tokyo, Japan

\*For reprints and all correspondence: Seiichiro Ozono, Department of Urology, Hamamatsu University School of Medicine, 1-20-1 Handayama, Higashi-ku, Hamamatsu, Shizuoka 431-3192, Japan. E-mail: oznsei@hama-med.ac.jp

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## Abstract

**Objective:** To evaluate the efficacy and safety of degarelix 3-month depot in Japanese patients with prostate cancer.

**Methods:** In this Phase II, open-label, parallel-group study, 155 Japanese prostate cancer patients were randomized to treatment with degarelix administered subcutaneously at a maintenance dose of 360 or 480 mg every 84 days for 12 months, after receiving an initial dose of 240 mg. The primary endpoint was the cumulative probability of serum testosterone  $\leq 0.5$  ng/ml (Days 28–364). Secondary endpoints included percent change in serum prostate-specific antigen level and proportion of patients with prostate-specific antigen failure at Day 364. For safety, adverse events were evaluated.

**Results:** The cumulative probability of serum testosterone  $\leq 0.5$  ng/ml (Days 28–364) was 88.3% (95% confidence interval: 77.9–94.0%) and 97.2% (95% confidence interval: 89.4–99.3%) in the 360 and 480 mg groups, respectively. The median percent change in serum prostate-specific antigen level from baseline to Day 364 was –95.05% and –96.43% in the 360 and 480 mg groups, respectively; the proportion of patients with prostate-specific antigen failure was 2.7% and 1.3%. The most frequent adverse event was injection site reaction; however, this did not cause any patient to discontinue treatment.

**Conclusions:** The 3-month dosing regimen of degarelix 360/480 mg was effective and well tolerated for treatment of Japanese prostate cancer patients. The 480 mg group showed a higher cumulative castration rate than the 360 mg group; thus, 480 mg was considered to be the optimal clinical dosage for future Phase III trials.

**Key words:** clinical trial, gonadotropin-releasing hormone antagonist, degarelix, Japan, prostate cancer

## Introduction

Prostate cancer is one of the most common cancers among men, and >1 100 000 new cases and 300 000 deaths are reported worldwide each year (1). In Japan, the estimated number of prostate cancer cases was 17 013 with an age-standardized incidence and mortality of 10.6 and 9.5, respectively, per 100 000 population in 2012 (2). It is predicted that in Japan, the incidence of prostate cancer will overtake that of gastric cancer. In 2015, prostate cancer will be the most common cancer among Japanese men (3).

Endocrine therapy with androgen deprivation therapy is one of the standard treatments for prostate cancer, and it is mainly used for the first-line treatment of metastatic prostate cancer. The most widely used androgen deprivation therapy involves the use of gonadotropin-releasing hormone (GnRH) agonists; however, there are some disadvantages caused by their mechanism of action, such as initial testosterone surge and potential microsurgers upon repeat administration. To avoid clinical flares caused by testosterone surges, the use of concomitant antiandrogens, such as bicalutamide, is often required in patients treated with GnRH agonists (4,5).

Degarelix, a new GnRH antagonist, was developed to avoid the testosterone surges caused by GnRH agonists. Its mechanism of action involves blocking GnRH receptors in the anterior pituitary gland, causing decreased secretion of both luteinizing hormone (LH) and follicle-stimulating hormone (FSH), and subsequently leading to a rapid suppression of testosterone (6). In addition, a more rapid induction of prostate-specific antigen (PSA) suppression has been found in patients treated with degarelix compared with those treated with leuporelin, a GnRH agonist (6–8). A 1-month regimen of degarelix was approved in the USA and Europe in 2008 and 2009, respectively, based on the results of a Phase III study (Study CS21) (6). In 2012, it was approved in Japan based on the results of the Study CS21 and a Japanese Phase II study (Study CL-0003) (9). An overseas Phase II study (Study CS18) (10) of a 3-month regimen of degarelix showed favorable results. In clinical practice, the 3-month regimen of GnRH agonists is used more frequently than the 1-month regimen in Western countries and Japan. Therefore, the aim of the present study was to evaluate the efficacy and safety of the 3-month regimen of degarelix in Japanese patients with prostate cancer.

## Patients and methods

### Study design and patients

This Phase II, randomized, open-label, parallel-group study was conducted in 30 sites in Japan from October 2010 to April 2012. The study design is shown in Fig. 1. The Institutional Review Board at each study site approved the study protocol. This study was conducted in accordance with the Good Clinical Practice, International Conference on Harmonization guidelines and the Declaration of Helsinki. Written informed consent was obtained from each patient prior to the study start.

Patients fulfilling the following criteria at screening were enrolled in the study: men aged 20 years or older at the time of providing consent, with histologically proven prostate cancer (adenocarcinoma) at any stage, in whom endocrine treatment was indicated (including those with rising serum PSA after undergoing prostatectomy or radiotherapy); serum testosterone > 2.2 ng/ml at screening; Eastern Cooperative Oncology Group Performance Status score of 0–2 and serum PSA ≥ 2 ng/ml at screening. Exclusion criteria were as follows: patients receiving previous or present endocrine treatment for prostate cancer or candidates for curative therapy including radical prostatectomy or radiotherapy within 12 months of the study start.

### Randomization and treatment

After final registration at Bellsystem24 (Tokyo, Japan), patients were randomly assigned in a 1:1 ratio to treatment by the minimization method using the following four items as assignment factors: age at the time of obtaining informed consent (<75 years, ≥75 years), prior treatment of prostate cancer, disease stage at the final registration and serum PSA at screening (<20 ng/ml, ≥20 ng/ml). After a 21-day screening period, degarelix was initially administered subcutaneously at a dose of 240 mg (40 mg/ml) to all the patients. Starting on Day 28 after the initial administration, patients were treated with degarelix administered subcutaneously at a maintenance dose of 360 mg (60 mg/ml) or 480 mg (60 mg/ml) every 84 days for a total of four doses (a total of 12 months of treatment). The prohibited concomitant drugs and therapies were GnRH agonists, GnRH antagonists, antiandrogens or estrogens, and 5α-reductase inhibitors; surgical castration and radical prostatectomy; and radiotherapy.

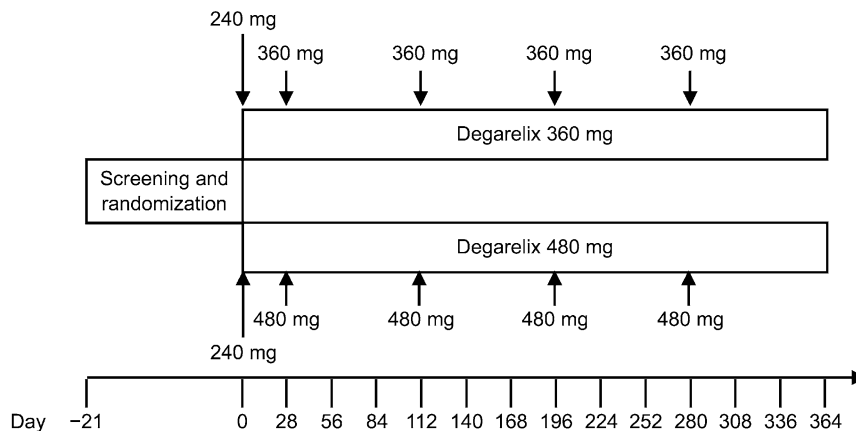


Figure 1. Clinical trial design.

### Efficacy assessments

The primary endpoint was the cumulative probability of serum testosterone  $\leq 0.5$  ng/ml from Days 28 to 364. A serum testosterone level  $> 0.5$  ng/ml was regarded as treatment failure.

Secondary endpoints were the proportion of patients with a serum testosterone level  $\leq 0.5$  ng/ml from Days 28 to 364, the percent change in serum PSA level at Days 28 and 364, and the proportion of patients with PSA failure (serum PSA relapse) from Days 0 to 364. Additionally, the following pharmacodynamic parameters (from Days 0 to 364) were evaluated: serum testosterone level (time course change), serum PSA level (percent change) and serum LH and FSH levels (time course change). Serum levels of testosterone, PSA, LH and FSH were determined as reported previously (9).

### Safety assessments

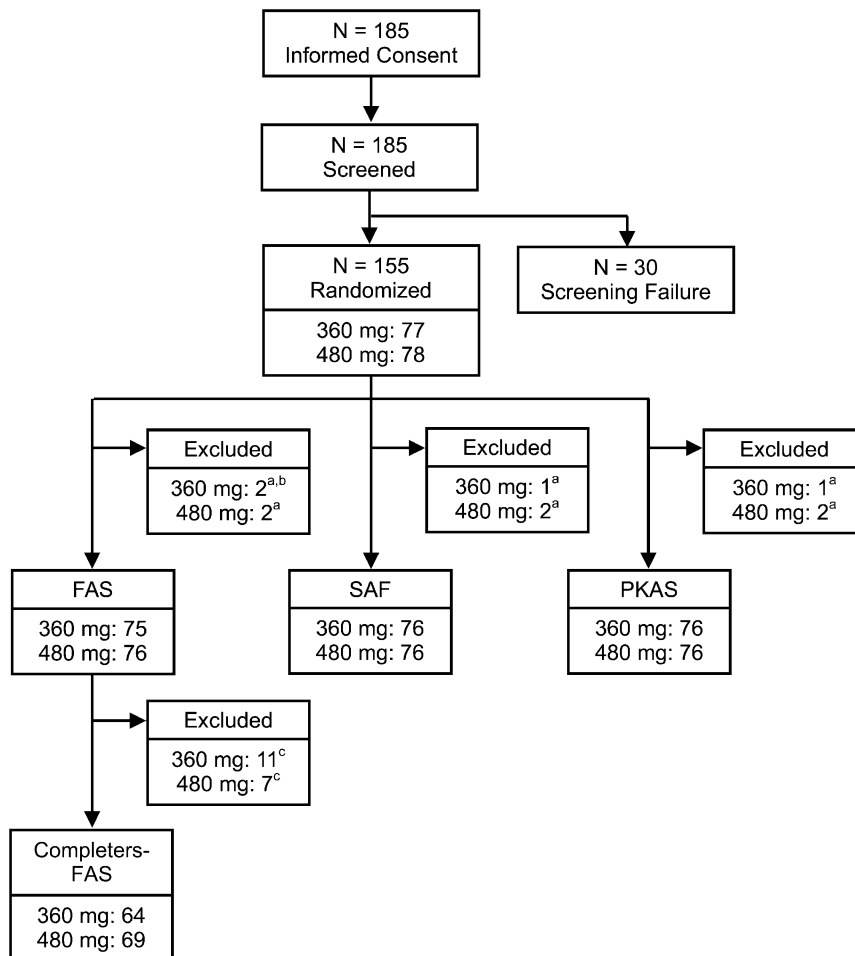
The safety assessments were adverse events (AEs); serious AEs; adverse drug reactions (ADRs), including injection site reactions; laboratory values, including biochemistry, hematology and urinalysis; vital signs and 12-lead electrocardiograms. AEs were graded in accordance with the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), version 4.0.

### Pharmacokinetic assessments

Plasma concentrations of degarelix were determined by Covance Laboratories Ltd. (Harrogate, UK) using a validated liquid chromatography-tandem mass spectrometry method. The limit of quantitation for degarelix in plasma was 0.5 ng/ml. The plasma samples were taken every 28 days throughout the study period. The trough plasma concentration of degarelix ( $C_{\text{trough}}$ ) was measured on Days 28, 112, 196, 280 and 364. Additionally, the plasma samples were also taken 3 and 7 days after Day 28 from a subset of subjects, and the maximum observed plasma concentration ( $C_{\text{max}}$ ) and elapsed time to attain  $C_{\text{max}}$  after a dose on Day 28 ( $T_{\text{max}}$ ) were calculated.

### Statistical analysis

The planned sample size was 120 subjects (60 each in the degarelix 360 and 480 mg maintenance-dose groups) based on the sample size of the Study CS18 rather than based on a statistical sample size design, in order to confirm whether the present study findings are similar to those of Study CS18. In summary, assuming that in both treatment arms, there is an annual 15% drop-out, if the true response rates in the two treatment regimens are assumed to be 90% and 95%, respectively, then in a study with 60 patients/arm, there is approximately an 84% chance that the highest response will be observed in



**Figure 2.** Patient disposition. FAS, full analysis set; PKAS, pharmacokinetic analysis set; SAF, safety analysis set.

<sup>a</sup>No test drug administration. <sup>b</sup>Lack of efficacy parameters. <sup>c</sup>Discontinued and no testosterone  $> 0.5$  ng/ml.

the arm with the highest true response rate. The populations for analysis were the full analysis set (FAS), completers–FAS, safety analysis set (SAF) and the pharmacokinetic analysis set (PKAS). The FAS was defined as subjects diagnosed with prostate cancer in whom the study drug was administered and at least one efficacy variable was evaluated after administration. The completers–FAS was defined as subjects who completed the study or showed a serum testosterone level exceeding 0.5 ng/ml after Day 28 of treatment. The SAF was defined as subjects who received the study drug. The PKAS was defined as subjects who received the study drug and from whom a sample for drug concentration measurement was collected at one or more time points.

Descriptive statistics were used to describe patient baseline characteristics and pharmacokinetic parameters. For the FAS, the cumulative probability of serum testosterone  $\leq 0.5$  ng/ml from Days 28 to 364 (primary endpoint) was estimated using the Kaplan–Meier method by considering a serum testosterone level of  $> 0.5$  ng/ml from Days 28 to 364 of treatment as the event of interest. The two-sided 95% confidence intervals (CIs) were calculated with the Greenwood formula. The percent change in serum PSA was calculated in the FAS. The proportion of subjects with PSA failure and the two-sided 95% CI were calculated. The accumulated incidence was estimated using the Kaplan–Meier method by considering serum PSA relapse as the event of interest. For the completers–FAS population, the proportion of subjects in whom serum testosterone was suppressed to  $\leq 0.5$  ng/ml from Days 28 to 364 of treatment (proportion of castration) and the two-sided 95% confidence interval (Clopper–Pearson confidence interval) was calculated. The frequency of AEs and ADRs was tabulated according to System Organ Class and Preferred Term of MedDRA. For the pharmacokinetic assessment of the accumulation of degarelix, the geometric mean ratios (GMRs) and the 95% CIs of each  $C_{\text{trough}}$  measured at each evaluation time were compared in each treatment group. As no statistical test was planned in the CS18 study, statistical significance was not evaluated in the present study. All statistical analyses, including pharmacokinetic parameter calculations, were performed using SAS, version 9.1.3 (SAS Institute, Cary, NC, USA).

## Results

### Patients

The disposition of patients is shown in Fig. 2. In total, 185 patients were screened, and 77 and 78 patients were randomized to the 360 and 480 mg groups, respectively. One and two patients in the 360 and 480 mg groups, respectively, discontinued before the initial test drug injection. Sixteen patients in the 360 mg group discontinued treatment for the following reasons: AEs, 3 patients; lack of efficacy, 11 patients (increase or insufficient decrease in the PSA level in 9 patients and increase in the testosterone and PSA level in 2 patients) and withdrawal of consent, 2 patients. Seven patients in the 480 mg group discontinued treatment for the following reasons: AE, one patient; lack of efficacy, five patients (increase or insufficient decrease in the PSA level in five patients) and other, one patient.

The baseline characteristics of the patients are shown in Table 1. There were no remarkable differences in the patient characteristics between both groups.

### Efficacy

**Primary endpoint:** The cumulative probability of serum testosterone  $\leq 0.5$  ng/ml from Days 28 to 364 (FAS) was 88.3% (95% CI: 77.9–94.0%) in the 360 mg group and 97.2% (95% CI: 89.4–99.3%) in the 480 mg group.

**Table 1.** Patient baseline characteristics (FAS)

	Degarelix 360 mg group (N = 75)	Degarelix 480 mg group (N = 76)
Age, years	74.3 $\pm$ 6.68	73.3 $\pm$ 6.26
Weight, kg	61.63 $\pm$ 7.92	64.26 $\pm$ 8.87
Body mass index, kg/m <sup>2</sup>	23.35 $\pm$ 2.47	24.07 $\pm$ 2.90
Prior treatment for prostate cancer		
Overall	7 (9.3)	7 (9.2)
Prostatic extirpation	2 (2.7)	2 (2.6)
Chemoradiotherapy	2 (2.7)	2 (2.6)
Neoadjuvant/adjuvant therapy	0 (0)	0 (0)
Other therapy	0 (0)	0 (0)
Watchful waiting	4 (5.3)	5 (6.6)
Eastern Cooperative Oncology Group Performance Status		
0	70 (93.3)	74 (97.4)
1	5 (6.7)	2 (2.6)
Stage of prostate cancer at date of registration		
Localized	44 (58.7)	44 (57.9)
Locally advanced	20 (26.7)	19 (25.0)
Metastatic	9 (12.0)	11 (14.5)
Not classifiable	2 (2.7)	2 (2.6)
PSA, ng/ml		
$< 20$	48 (64.0)	49 (64.5)
$\geq 20$	27 (36.0)	27 (35.5)
Testosterone, ng/ml		
$< 3.5$	16 (21.3)	15 (19.7)
3.5–4.9	29 (38.7)	36 (47.4)
$\geq 5.0$	30 (40.0)	25 (32.9)

Data are presented as mean  $\pm$  SD or n (%).

FAS, full analysis set; PSA, prostate-specific antigen.

**Secondary endpoints:** The proportion of patients with a serum testosterone level  $\leq 0.5$  ng/ml from Days 28 to 364 was 87.50% (95% CI: 76.85–94.45%) in the 360 mg group and 97.10% (95% CI: 89.92–99.65%) in the 480 mg group (completers–FAS). The time to treatment failure (serum testosterone  $> 0.5$  ng/ml) is shown in Fig. 3. The median percent change in serum PSA level from baseline to Day 28 was  $-70.4\%$  and  $-79.9\%$  in the 360 and 480 mg groups, respectively. The proportion of patients with PSA failure (serum PSA relapse) from baseline to Day 364 was 2.7% and 1.3% in the 360 and 480 mg groups, respectively.

Regarding the pharmacodynamic assessments, the median time course change in serum testosterone and median percent change in serum PSA levels from baseline to Day 364 are shown in Fig. 4a and b, respectively. Both the 360 and 480 mg groups showed  $> 70\%$  reduction in serum PSA level within 4 weeks from the first dose. The median percent change in serum PSA level from baseline to Day 364 was  $-95.05\%$  (range,  $-99.9\%$ ,  $-51.3\%$ ) in the 360 mg group and  $-96.43\%$  (range,  $-99.9\%$ ,  $-44.0\%$ ) in the 480 mg group. The median time course change in serum LH and FSH levels from baseline to Day 364 is shown in Fig. 5a and b, respectively.

### Safety

The overall incidence of AEs was 94.7% (72/76) and 96.1% (73/76) in the 360 and 480 mg groups, respectively. Serious AEs occurred in 17.1% (13/76) and 9.2% (7/76) of patients in each group, respectively. The incidence of ADRs was 89.5% (68/76) and 93.4% (71/76) in the 360 and 480 mg groups, respectively. The treatment-emergent AEs with an incidence of  $\geq 10\%$  in any group are shown in Table 2. The most frequently observed AEs were injection site reactions, hot flush, nasopharyngitis, weight increase, and pyrexia in the 360 mg

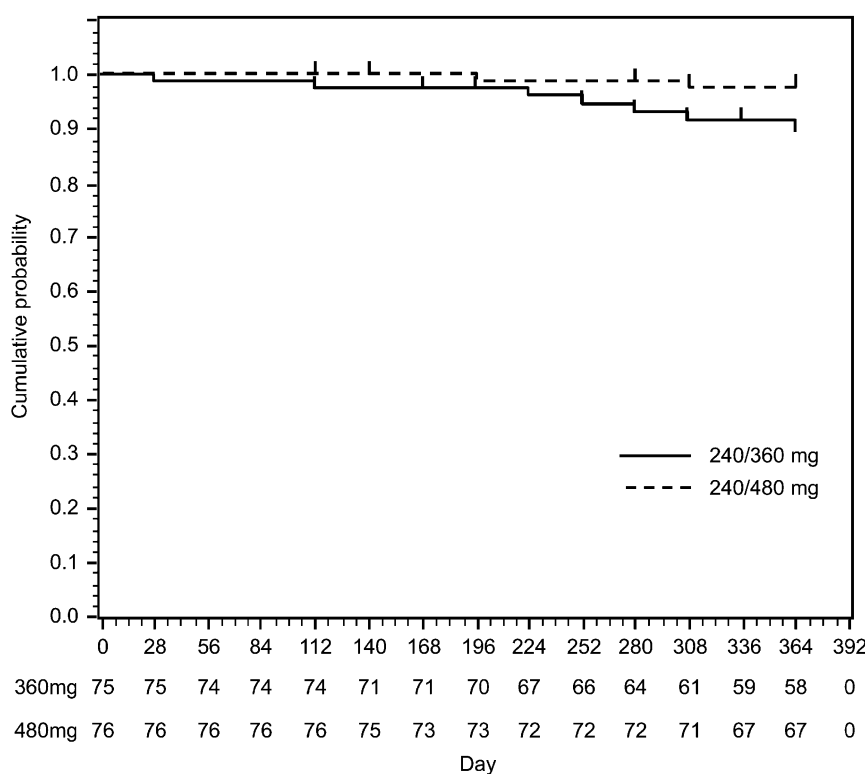


Figure 3. Time to serum testosterone > 0.5 ng/ml from Days 28 to 364 (FAS).

group, and injection site reactions, hot flush, nasopharyngitis, pyrexia, weight increase, and malaise in the 480 mg group. In this study, 50.0% and 60.5% of patients in the 360 and 480 mg groups, respectively, showed AEs related to injection site reactions. However, no patient discontinued the treatment because of injection site reactions. All injection site reactions were mild or moderate (Grade 1 or 2). One patient in the 360 mg group died; this patient committed suicide after the initial administration of the study drug, but before the maintenance dose was administered. There were no apparent clinically significant changes in laboratory evaluations and vital signs. Regarding the 12-lead electrocardiogram evaluation, one patient in the 480 mg group showed a marked increase ( $\geq 480$  ms) in QTcF on Day 364.

### Pharmacokinetics

The mean  $\pm$  SD plasma concentration–time curves for degarelix are shown in Fig. 6. Overall, the mean plasma concentrations of degarelix in the 480 mg group were higher than those in the 360 mg group. The GMR (95% CI) of  $C_{\text{trough}}$  values between Days 28 and 364 were 1.258 (1.114–1.421) and 1.752 (1.589–1.932) in the 360 and 480 mg groups, respectively, and the plasma concentration of degarelix in both dose groups did not achieve steady state by Day 364. Data from the subset of subjects showed that degarelix were absorbed and distributed rapidly after the maintenance dose with a median  $T_{\text{max}}$  of 2.97 days and 2.95 days and a mean  $\pm$  SD  $C_{\text{max}}$  of  $74.69 \pm 29.96$  and  $98.53 \pm 31.69$  ng/ml in the 360 mg ( $N = 36$ ) and 480 mg ( $N = 39$ ) groups, respectively.

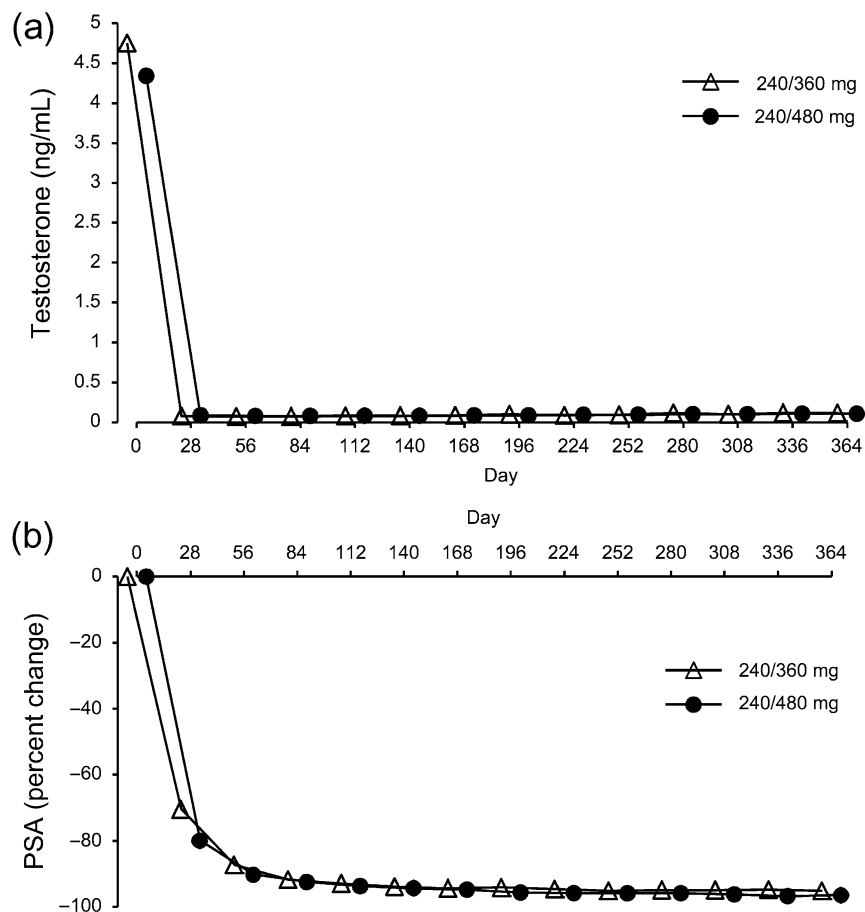
### Discussion

This is the first study to evaluate the efficacy and safety of the 3-month dosing regimen of degarelix in Japanese patients with

prostate cancer. In this study, patients were randomized to treatment with degarelix given at a maintenance dose of 360 or 480 mg every 84 days for up to 12 months. Patients with localized or locally advanced prostate cancer, not only those with metastatic disease, were enrolled in the present study for treatment with degarelix, in accordance with the clinical practice in Japan of providing endocrine therapy to prostate cancer patients at any stage of the disease (9).

The efficacy of the 3-month dosing regimen of degarelix in terms of the cumulative probability of serum testosterone  $\leq 0.5$  ng/ml (primary endpoint) in the 480 mg group was similar to that of the overseas Phase II study (Study CS18) of the 3-month regimen (89.0% and 93.3% in the 360 and 480 mg groups, respectively) (10) and the Japanese Phase II study of the 1-month regimen (Study CL-0003) (94.5% and 95.2% in the 80 and 160 mg maintenance-dose groups, respectively) (9). Two previous studies (11,12) also showed that a 3-month dosing formulation of LH-releasing hormone agonists was effective in reducing serum testosterone to the castration range/level in Japanese prostate cancer patients. In a leuprorelin study (12), the castration level was reached in 100% of patients; however, this study used a higher castration level (testosterone  $< 1$  ng/ml), and the follow-up duration was shorter (24 weeks). In the present study, the proportion of patients with satisfactory testosterone suppression at Day 364 in the 480 mg group was higher than that of the 360 mg group, and the  $C_{\text{trough}}$  at Day 364 in the 480 mg group was higher than that in the 360 mg group as well.

Both the 360 and 480 mg groups showed decreased levels of serum PSA after administration of the study drug from the perspective of 'percent change in PSA at Day 28 and Day 364' and 'proportion of patients with PSA failure from Days 0 to 364'. In the Japanese Phase II study of the 1-month regimen (Study CL-0003), the incidence of PSA failure was 7.4% and 7.3% in the 80 and 160 mg maintenance-dose



**Figure 4.** Median time course change of (a) serum testosterone and (b) median percent change of prostate-specific antigen (PSA) from baseline to Day 364 (FAS).

groups, respectively (9). These values were relatively higher than those of the present study (2.7% and 1.3% in the 360 and 480 mg group, respectively). In the Japanese Phase II study of the 1-month regimen (Study CL-0003), the percent change in PSA at Day 28 (-80.14% and -79.52% in the 80 and 160 mg maintenance-dose groups, respectively) was comparable to the findings of the present study (9). These findings suggest that patients could benefit equally from 1- and 3-month regimens of degarelix by lowering the incidence of PSA failure; however, further comparative study of the 1- and 3-month regimen of degarelix would be warranted in the Japanese population. Furthermore, differences in the definitions of PSA failure, follow-up duration, and timing of the evaluations in this study and the GnRH agonist studies (11,12) make these studies difficult to compare, and further studies comparing the efficacy of 3-month regimens of degarelix and GnRH agonists are warranted.

The time course change of serum FSH level by degarelix differs from that by the GnRH agonist, leuprolerin acetate, because of their different mechanisms of action, as evidenced in the results of the overseas Phase III study of the 1-month regimen (Study CS21) (6) and a study of Japanese prostate cancer patients who were switched from degarelix to leuprolerin (13). In the present study, degarelix decreased serum FSH levels as well as serum LH levels during 1 year, which is consistent with the findings of the overseas Phase III study of the 1-month regimen (Study CS21) (6). The serum FSH level has been found to be associated with the extraprostatic extension of prostate cancer (14) and the time to development of castration-resistant prostate cancer (15). These findings suggest that

there may be a therapeutic benefit in blocking FSH and/or FSH receptor signaling in prostate cancer patients.

In the present study, both the 360 and 480 mg doses were well tolerated. The most frequently observed AEs involved injection site reactions; however, all were Grade 1 or 2 (no Grade 3 reactions). Injection site reactions were more frequently observed in the present study than in the Japanese Phase II study of the 1-month regimen (Study CL-0003), because of the following differences between the 1- and 3-month regimens. First, the number of sites for maintenance-dose administration differs, as there is only one site required for the 1-month regimen, and two sites are required for the 3-month regimen. Second, the maintenance doses differ as 20 mg/ml of degarelix are used for the 1-month regimen and 60 mg/ml are used for the 3-month regimen. Although the incidence of injection site reactions was higher than that in patients treated with the 1-month dosing regimen, they did not cause the discontinuation of the study drug. Other frequently observed AEs were hot flush, weight increase, nasopharyngitis and malaise. Hot flush and weight increase, which have been previously reported in patients treated with GnRH antagonists (6,9), have been shown to be associated with a decrease in testosterone (16).

Although the overseas CS18 study showed that the incidences of AEs after maintenance doses of 360 and 480 mg did not greatly exceed the incidence of AEs after the initial dose of 240 mg, the maintenance doses were to be administered for the first time in Japan. Accordingly, the present study included a subset of subjects who attended extra visits (3 and 7 days after Day 28) with the purpose of performing safety assessments. However, the data and safety

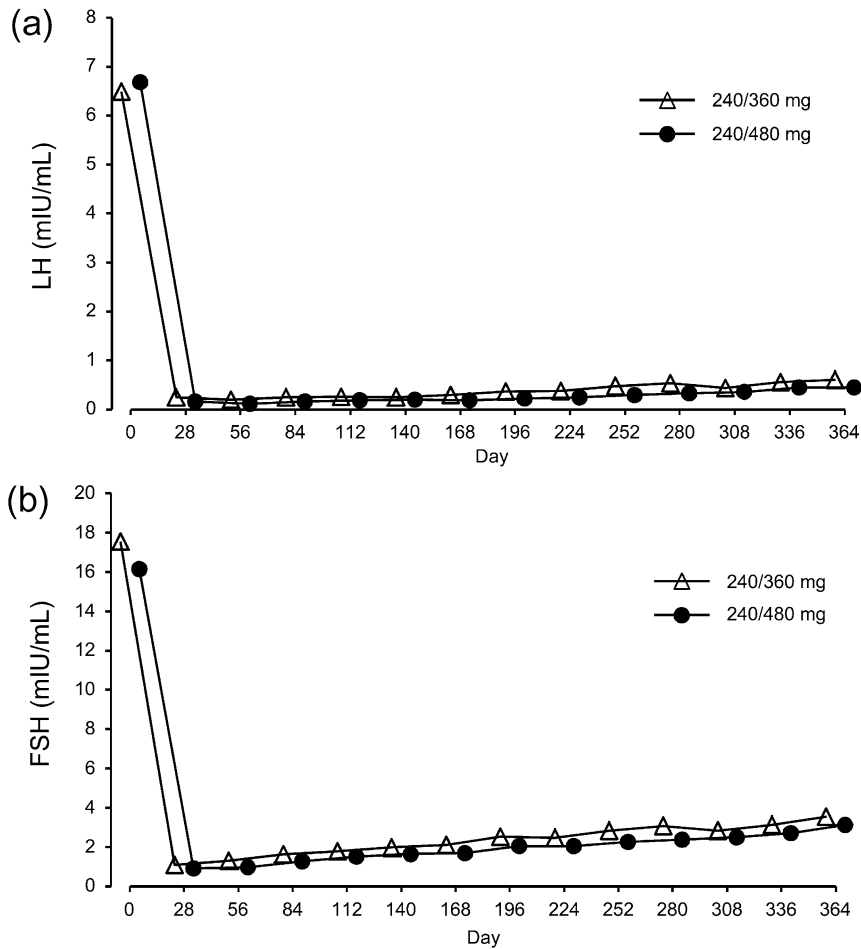


Figure 5. Median time course change in (a) serum luteinizing hormone (LH) and (b) follicle-stimulating hormone (FSH) levels from baseline to Day 364 (FAS).

Table 2. Incidence of treatment-emergent AEs ( $\geq 10\%$  in any group) (SAF)

	Degarelix 360 mg group (N = 76)	Degarelix 480 mg group (N = 76)
Injection site reaction		
Injection site pain	32 (42.1)	40 (52.6)
Injection site erythema	29 (38.2)	31 (40.8)
Injection site swelling	17 (22.4)	24 (31.6)
Injection site induration	15 (19.7)	15 (19.7)
Injection site mass	10 (13.2)	12 (15.8)
Hot flush	28 (36.8)	30 (39.5)
Nasopharyngitis	19 (25.0)	25 (32.9)
Weight increase	13 (17.1)	10 (13.2)
Pyrexia	9 (11.8)	21 (27.6)
Malaise	2 (2.6)	8 (10.5)

Data are presented as *n* (%).

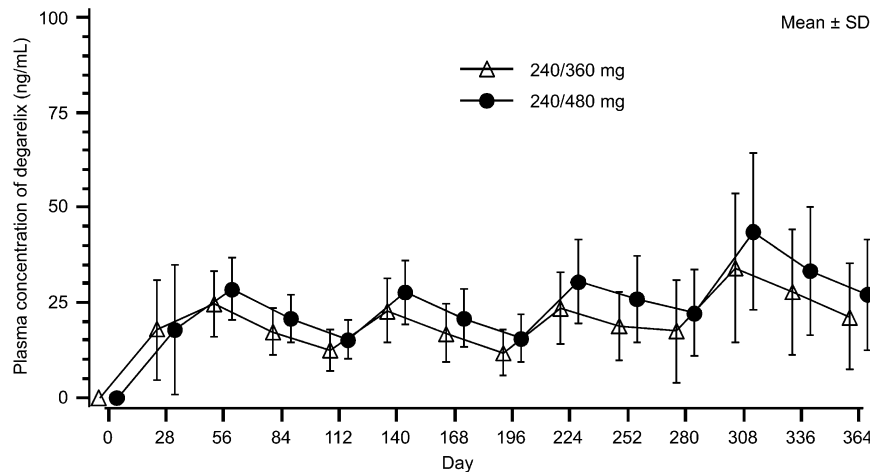
SAF, safety analysis set; AEs, adverse events.

monitoring committee evaluated the safety (injection site reactions of Grade 3 or higher and serious ADRs) in the first 12 patients allocated to the maintenance dose of 360 mg (60 mg/ml) or 480 mg (60 mg/ml), and judged that there were no significant safety concerns. Those extra visits were therefore canceled for the subsequent patients.

There has been some debate on the use of androgen deprivation therapy in prostate cancer patients with a history of cardiovascular disease because of a possible association between androgen deprivation therapy and high cardiovascular risk (17). Androgen deprivation therapy has also been associated with a high risk of dementia (18). When comparing different androgen deprivation therapies, treatment with GnRH agonists has been associated with a higher risk of cardiovascular events as well as other AEs compared with surgery (e.g. orchiectomy) (19,20). Albertsen et al. performed a pooled analysis of six Phase III prospective randomized trials to compare the cardiovascular morbidity between patients treated with GnRH agonists and antagonists. The findings revealed that the risk of cardiovascular events was significantly lower in prostate cancer patients treated with GnRH antagonists than in those treated with GnRH agonists, particularly among patients with a history of cardiovascular disease (21). Long-term studies with a large sample size are warranted to confirm the effect of androgen deprivation therapy on cardiovascular mortality and dementia.

The finding that  $C_{\text{trough}}$  values increased throughout the study period was apparently different from that of the Japanese Phase II study of the 1-month regimen (Study CL-0003) (22). The mechanism through which  $C_{\text{trough}}$  values increase is not entirely clear.

The present study has some limitations. First, since this study only included Japanese patients, our findings cannot be generalized to other ethnic populations. Second, there was no comparator, and



**Figure 6.** Mean plasma concentration–time curves for degarelix (PKAS).

this was not a confirmatory study. Finally, the dosing duration was limited. Studies to confirm the efficacy and to evaluate the long-term safety, pharmacokinetics and pharmacodynamics of degarelix 3-month depot with an active comparator are warranted in the future.

In conclusion, in this Phase II study of the 3-month dosing regimen of degarelix, both the 360 and 480 mg doses were found to be effective for the treatment of Japanese patients with prostate cancer, although the 480 mg dose was clinically superior to the 360 mg dose in this study. In particular, the 480 mg group showed a higher cumulative castration rate than the 360 mg group. Both 3-month dosing regimens were well tolerated among Japanese patients with prostate cancer. The optimal clinical dosage for future Phase III trials was determined to be 480 mg.

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## Conflict of interest statement

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