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ORIGINAL ARTICLE

# Cost-Effectiveness Analysis of Leuprorelin Acetate Atrigel in the Treatment of Prostate Cancer

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**OBJECTIVE**

This study aimed to evaluate the clinical effectiveness and cost of leuprorelin acetate Atrigel (Eligard®) in prostate cancer treatment and calculate its cost-effectiveness compared with other luteinizing hormone-releasing hormone (LHRH) agonists (leuprolide acetate microsphere [Lucrin®], goserelin [Zoladex LA®], and triptorelin [Decapeptyl®]).

**METHODS**

The primary health-related outcome was life-years gained, and effectiveness was measured through the difference between treatment options. Analyses were performed separately for testosterone suppression targets of <20 ng/dL and <50 ng/dL for disease risk groups (intermediate and high risk) and for disease periods (relapse-free, postrelapse, and postdistant metastasis). Only direct treatment costs were used for cost analyses. Resource utilization was estimated according to the National Comprehensive Cancer Network guidelines and expert opinion.

**RESULTS**

This study included 173 patients treated with definitive radiotherapy and maximal androgen blockade. The median follow-up duration was 125.37 (range 10.84-214.37) months. The percentages of patients whose testosterone levels decreased to <20 ng/dL and <50 ng/dL were higher with leuprorelin acetate Atrigel. Compared with leuprolide acetate microsphere, goserelin, and triptorelin, Leuprorelin acetate Atrigel provided cost savings of 8386.04 Turkish liras (TL), 3710.79 TL, and 8446.64 TL, respectively, in patients with testosterone levels of <20 ng/dL and 479.41 TL, 1142.13 TL, and 5490.79 TL, respectively, in patients with testosterone levels of <50 ng/dL. Deterministic sensitivity analysis showed that leuprorelin acetate Atrigel was superior to its comparators regarding incremental cost-effectiveness ratios at low- and high-sensitivity margins.

**CONCLUSION**

Leuprorelin acetate Atrigel was found to be clinically more effective and cost-saving than other LHRH agonists in the intermediate- and high-risk groups, regardless of testosterone suppression targets.

**Keywords:** Cost-saving; luteinizing hormone-releasing hormone agonist; pharmacoeconomics; testosterone suppression target.



## Introduction

Prostate cancer is one of the most commonly diagnosed cancers according to the GLOBOCAN data. [1] In Turkey, prostate cancer is the second most frequently diagnosed cancer in males, with an age-standardized incidence rate of 32.9 per 100.000 population, according to the Turkey Ministry of Health Cancer

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Statistics.[2] According to the National Cancer Institute, approximately 77% of the cases were reported to have localized and 13% regional disease at a diagnosis the estimated 5-year survival rate in those patients was 100%, while it was 98% for all disease stages.3 Prostate cancer is most frequently diagnosed in older males (aged 65-74 years).[3] As the proportion of older age groups increase in population demographics, the burden of prostate cancer on public health and healthcare systems also grows in parallel. Projections about the cost of treatment for prostate cancer in 2020 in the United States have indicated that it will be >$16 billion, compared to approximately $12 billion in 2010.[4]

Currently, the treatment of locally advanced prostate cancer is based on androgen deprivation therapy (ADT) and radiotherapy, as testosterone induces the growth of prostate cancer tissue. ADT focuses on reducing serum testosterone levels to the point that would be reached with surgical castration.[5] Current guidelines on prostate cancer define the castration levels of testosterone as <20 ng/dL after more precise laboratory tests were developed to measure the testosterone levels [6] and studies have shown that higher levels of serum testosterone in patients with advanced prostate cancer are associated with increased mortality.[7,8] However, the castrate level considered by the regulatory authorities and in clinical trials addressing castration in prostate cancer is still <50 ng/dL.[6] Testosterone levels <20 ng/dL are associated with a significantly lower risk of death compared with testosterone levels of ≥20 ng/dL.[7–10] The most common method of ADT is the use of synthetic peptides that mimic natural luteinizing hormone-releasing hormone (LHRH), namely LHRH agonists.

LHRH agonists have a high affinity for the gonadotropic-releasing hormone receptor and benefit from longer half-lives than natural LHRH agonists.[5] LHRH agonists have become a standard treatment for locally advanced and advanced prostate cancer as effectiveness is higher than antiandrogen monotherapy.[11]

Leuprorelin or leuprolide acetate is one of the most widely prescribed LHRH agonists, due to its favorable tolerability, and has been used for several years in the treatment of prostate cancer. Leuprorelin acetate Atrigel, a second-generation LHRH agonist, has been developed to reach lower castrate testosterone levels than conventional LHRH agonists.[12] In Turkey, the 3-month subcutaneous formulation of leuprorelin acetate Atrigel (Eligard®) contains 22.5 mg of leuprorelin acetate (Eligard® 22.5 mg), whereas the 3-month subcutaneous/intramuscular formulation of leuprolide acetate microsphere (Lucrin®) contains 11.25 mg of leuprolide acetate (Lucrin® 11.25 mg). A comparison between leuprorelin acetate Atrigel (Eligard®) 7.5 mg 1-month formulation and leuprolide acetate microsphere (Lupron®) 7.5 mg 1-month formulation that is registered elsewhere has shown that the area under the curve is 1.9 times higher with leuprorelin acetate Atrigel for leuprolide acetate release; which means that leuprorelin acetate Atrigel has provided an additional 14 days of testosterone suppression.[13] Conventional LHRH agonists are known to fail to reach testosterone levels of <50 ng/dL by 2% to 17% and <20 ng/dL by 13% to 37% of patients5; however, analyses with leuproreline acetate Atrigel have shown that testosterone levels were suppressed to <20 ng/dL in 88.3% to 97.5% of the patients with 1-, 3-, 4-, and 6-month formulations, respectively.[12]

The present study aims to evaluate the clinical effectiveness and cost of leuprorelin acetate Atrigel (Eligard®, Astellas Pharmaceuticals, Turkey) in the treatment of prostate cancer and to calculate its cost-effectiveness compared with other LHRH agonists, including leuprolide acetate microsphere (Lucrin®, Abbvie Pharmaceuticals, Turkey), goserelin (Zoladex LA®, Astra Zeneca, Turkey), and triptorelin (Decapeptyl®, Ferring, Turkey).

## Materials and Methods

This study was conducted at the Hacettepe University, in the Faculty of Medicine in the Ankara province of Turkey and included 173 patients with prostate cancer treated with definitive conformal radiotherapy (3-dimensional conformal radiotherapy or intensity-modulated radiation therapy) with a total dose of 74 Gy to76 Gy in conventional fractionation and maximal androgen blockade. All patients uniformly received three months of neo-adjuvant and six months of adjuvant maximal androgen blockade. Patients were grouped as intermediate or high risk, according to the American Joint Committee on Cancer 2010 guidelines or Gleason score.[14,15] As almost all patients were covered by the social security system, direct cost-based cost-effectiveness analyses were performed from the government (Turkish Social Security Institution) perspective.

The primary outcome for health-related outcomes was life-years gained (LYG), which was calculated as the difference between the follow-up duration and calculated life expectancy for each patient (presented as life-years lost). Effectiveness of the treatment was measured through the difference in life-years lost among

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the treatment options. Target serum testosterone levels were also considered during the assessments and two separate analyses were performed for castration levels of testosterone of <20 ng/dL and <50 ng/dL.

Cost-effectiveness analyses were based on the estimated costs at three disease periods (relapse-free, postrelapse, and postdistant metastasis) and overall survival estimates. Both the costs and survival estimates were based on individual patient data. For estimating the direct costs of the treatment, a prostate biopsy was assumed to be performed at the beginning of the disease, 37-38 sessions of radiotherapy were assumed to be received by each patient (expert opinion), and LHRH treatments were assumed for six months for the intermediate-risk patients and 24 months for the high-risk patients.[16] Intermediate risk was defined as stage T2b, according to the American Joint Committee on Cancer guidelines, the Gleason score of 7, or prostate-specific antigen levels of >10 ng/mL and ≤20 ng/mL. High risk was defined as stage T2c, prostate-specific antigen levels of >20 ng/mL, or the Gleason score of ≥8.[14,15]

The prices and monthly costs of hormone therapy, chemotherapy, radiotherapy, and follow-up for each of three disease periods (relapse-free, postrelapse, and postdistant metastasis) were included in the model. Only direct costs were considered. Resource utilization was estimated in accordance with the National Comprehensive Cancer Network guidelines and expert opinion. The prices of medications and services were drawn from the list released by the Turkish Ministry of Health and the Social Security Institution.

The currency reported in this study was Turkish lira (TL) and the prices of the relevant medications and procedures were as of 12 November 2018. The willingness-to-pay threshold per LYG was set equal to the gross domestic product per capita, which was declared as 10.597 US dollars (49.806 TL; 1 US dollar=4.7 TL in mid-2018) for the year 2017 by the Turkish Statistical Institute. The study model is summarized in Figure 1.

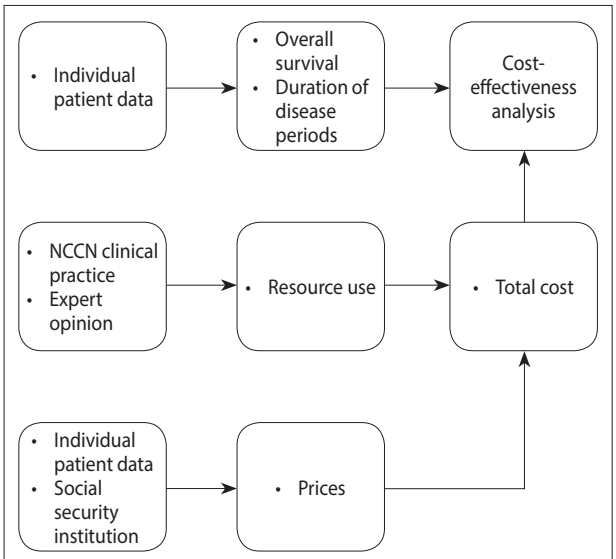


**Fig. 1.** Structure of the study model.

### Statistical Analysis

Data were analyzed using PASW Statistics for Windows, version 18.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were expressed as numbers and percentages for categorical variables and as median and minimum-maximum for numerical variables. Chi-square test and, when the condition for chi-square was not met, Fisher's exact test was used for the comparison of independent categorical variables. In multiple independent group comparisons, the Kruskal-Wallis test was used for non-normally distributed numerical variables. A P-value of <0.05 was considered statistically significant.

## Results

This study included 173 patients with prostate cancer. The median follow-up duration was 125.37 (range 10.84-214.37) months for the entire cohort. No clinically significant difference was obtained among the groups classified according to LHRH analogue type (Table 1). Distribution of the patients according to LHRH analogues, risk group, and serum testosterone levels are summarized in Table 2. In the intermediate-risk group, the proportion of patients whose serum testosterone levels were <20 ng/dL and <50 ng/dL with leuprorelin acetate Atrigel were 80% and 100%, respectively. The corresponding data were 33.3% and 77.8% for leuprolide acetate microsphere, respectively; 64% and 84% for goserelin, respectively; and 37.5% and 62.5% for triptorelin, respectively. In the high-risk group, the proportions of patients whose serum testosterone levels were <20 ng/dL and <50 ng/dL with leuprorelin acetate Atrigel were 90% and 100%, respectively. The corresponding data were 52.4% and 71.4% for leuprolide acetate microsphere, respectively; 53.3% and 81.3% for goserelin, respectively; and 40% and 66.7% for triptorelin, respectively.

When the costs of the treatments according to the risk groups and serum testosterone levels were evaluated for three disease periods (relapse-free, postre-

**Table 1** Patient characteristics classified by luteinizing hormone-releasing hormone agonists

| | Leuprorelin acetate Atrigel (n=20) | Leuprolide acetate microsphere (n=30) | Goserelin (n=100) | Triptorelin (n=23) | p |
|---|---|---|---|---|---|
| Age, y, median (min-max) | 70.5 (58-78) | 66 (55-75) | 69 (50-82) | 70 (53-78) | 0.125[a] |
| Gleason score, n (%) | | | | | |
| ≤6 | 5 (25) | 10 (33.3) | 36 (36.0) | 14 (60.9) | 0.170[b] |
| 7 | 11 (55.0) | 11 (36.7) | 39 (39.0) | 7 (30.4) | |
| ≥8 | 4 (20.0) | 9 (30.0) | 25 (25.0) | 2 (8.7) | |
| Risk group, n (%) | | | | | |
| Intermediate | 10 (50.0) | 9 (30.0) | 25 (25.0) | 8 (34.8) | 0.155[b] |
| High | 10 (50.0) | 21 (70.0) | 75 (75.0) | 15 (65.2) | |
| PSA level, n (%) | | | | | |
| <10 ng/mL | 9 (45.0) | 5 (16.7) | 26 (26.0) | 3 (13.0) | 0.086[b] |
| 10-20 ng/mL | 9 (45.0) | 17 (56.7) | 39 (39.0) | 12 (52.2) | |
| >20 ng/mL | 2 (10.0) | 8 (26.7) | 35 (35.0) | 8 (34.8) | |
| AJCC stage, n (%) | | | | | |
| T1 | 0 (0.0) | 1 (3.3) | 2 (2.0) | 0 (0.0) | 0.282[c] |
| T2a | 12 (60.0) | 13 (43.3) | 39 (39.0) | 10 (43.5) | |
| T2b | 0 (0.0) | 3 (10.0) | 9 (9.0) | 2 (8.7) | |
| T2c | 1 (5.0) | 1 (3.3) | 10 (10.0) | 4 (17.4) | |
| T3a | 3 (15.0) | 11 (36.7) | 32 (32.0) | 3 (13.0) | |
| T3b | 4 (20.0) | 1 (3.3) | 8 (8.0) | 4 (17.4) | |

[a]Kruskal-Wallis test; [b]Chi-square test; [c]Fisher's exact test. AJCC: American Joint Committee on Cancer; PSA: Prostate-specific antigen

**Table 2** Distribution of the patients according to luteinizing hormone-releasing hormone analogues by risk groups and serum testosterone levels

| | Intermediate-risk patients, n (%) | | | High-risk patients, n (%) | | |
|---|---|---|---|---|---|---|
| | Serum testosterone levels, ng/dL | | | | | |
| | <20 | ≥20 | Total | <20 | ≥20 | Total |
| Leuprorelin acetate atrigel | 8 (80) | 2 (20) | 10 (100) | 9 (90) | 1 (10) | 10 (100) |
| Leuprolide acetate microsphere | 3 (33.3) | 6 (66.7) | 9 (100) | 11 (52.4) | 10 (47.6) | 21 (100) |
| Goserelin | 16 (64) | 9 (36) | 25 (100) | 40 (53.3) | 35 (46.7) | 75 (100) |
| Triptorelin | 3 (37.5) | 5 (62.5) | 8 (100) | 6 (40) | 9 (60) | 15 (100) |
| Total | 30 (57.7) | 22 (42.3) | 52 (100) | 66 (54.5) | 55 (45.5) | 121 (100) |
| | <50 | ≥50 | Total | <50 | ≥50 | Total |
| Leuprorelin acetate atrigel | 10 (100) | 0 | 10 (100) | 10 (100) | 0 | 10 (100) |
| Leuprolide acetate microsphere | 7 (77.8) | 2 (22.2) | 9 (100) | 15 (71.4) | 6 (28.6) | 21 (100) |
| Goserelin | 21 (84) | 4 (16) | 25 (100) | 61 (81.3) | 14 (18.7) | 75 (100) |
| Triptorelin | 5 (62.5) | 3 (37.5) | 8 (100) | 10 (66.7) | 5 (33.3) | 15 (100) |
| Total | 43 (82.7) | 9 (17.3) | 52 (100) | 96 (79.3) | 25 (20.7) | 121 (100) |

lapse, and postdistant metastasis), the treatment costs for leuprorelin acetate Atrigel were found to be slightly lower than leuprolide acetate microsphere, but slightly higher than goserelin and triptorelin. The total costs, survival estimates, incremental cost-effectiveness ratios (ICERs), and net monetary benefit values according to the risk groups and serum testosterone levels are presented in Table 3. LYG with leuprorelin acetate Atrigel

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**Table 3** Treatment costs at an individual patient level

| | Testosterone target level <20 ng/dL | | | | Testosterone target level <50 ng/dL | | | |
|---|---|---|---|---|---|---|---|---|
| | Leuprorelin acetate atrigel | Leuprolide acetate microsphere | Goserelin | Triptorelin | Leuprorelin acetate atrigel | Leuprolide acetate microsphere | Goserelin | Triptorelin |
| Intermediate-risk group | | | | | | | | |
| LYG, years | 1.03 | 0.43 | 0.82 | 0.48 | 3.57 | 2.78 | 3.00 | 2.23 |
| Total costs, TL | 14999.00 | 24860.89 | 16881.98 | 22958.65 | 16385.17 | 20815.17 | 17871.39 | 22547.36 |
| Additional LYG with leuprorelin acetate atrigel, y | | 0.60 | 0.21 | 0.55 | | 0.79 | 0.57 | 1.34 |
| Cost difference, TL | | –9861.89 | –1882.98 | –7959.64 | | –4430.01 | –1486.22 | –6162.20 |
| Net monetary benefit, TL | | 39683.01 | 12,107.37 | 35118.17 | | 43964.68 | 29951.19 | 72876.96 |
| ICER, TL/LYG | | –16470.89 | –9172.54 | –14597.16 | | –5580.94 | –2600.48 | –4600.39 |
| High-risk group | | | | | | | | |
| LYG, y | 1.06 | 0.61 | 0.63 | 0.47 | 1.42 | 1.01 | 1.15 | 0.94 |
| Total costs, TL | 17656.11 | 25899.65 | 22517.95 | 26754.70 | 21041.07 | 26881.44 | 21954.69 | 26097.10 |
| Additional LYG with leuprorelin acetate atrigel, y | | 0.44 | 0.43 | 0.59 | | 0.40 | 0.26 | 0.47 |
| Cost difference, TL | | –8243.54 | –4861.84 | –9098.58 | | –5840.38 | –913.63 | –5056.03 |
| Net monetary benefit, TL | | 30216.16 | 26278.20 | 38302.71 | | 25983.48 | 14073.79 | 28556.32 |
| ICER, TL/LYG | | –18685.84 | –11306.70 | –15517.10 | | –14440.93 | –3457.71 | –10715.62 |
| All patients | | | | | | | | |
| LYG, years | 1.02 | 0.56 | 0.67 | 0.47 | 2.00 | 1.47 | 1.64 | 1.30 |
| Total costs, TL | 17236.06 | 25622.10 | 20946.85 | 25682.70 | 19626.33 | 25105.74 | 20768.47 | 25117.12 |
| Additional LYG with leuprorelin acetate atrigel, y | | 0.46 | 0.35 | 0.55 | | 0.53 | 0.36 | 0.70 |
| Cost difference, TL | | –8386.04 | –3710.79 | –8446.64 | | –5479.41 | –1142.13 | –5490.79 |
| Net monetary benefit, TL | | 31351.72 | 21084.83 | 35927.32 | | 32018.55 | 19056.05 | 40107.07 |
| ICER, TL/LYG | | –18186.88 | –10637.67 | –15308.67 | | –10283.18 | –3175.47 | –7900.16 |

versus no LHRH agonists was superior to other medications versus no LHRH agonists. Similarly, total treatment costs for leuprorelin acetate Atrigel were all lower than other LHRH agonists, which yielded significant net monetary benefits and ICER values in both risk groups for all testosterone levels. Cost-effectiveness analyses showed that leuprorelin acetate Atrigel provided savings of 9861.89 TL, 1882.98 TL, and 7959.64 TL against leuprolide acetate microsphere, goserelin, and triptorelin, respectively, in the intermediate-risk patients whose testosterone suppression target was <20 ng/dL. For the patients in the intermediate-risk group whose testosterone suppression target was <50 ng/dL, these savings were 4430.01 TL, 1486.22 TL, and 6162.20 TL, respectively.

In high-risk patients, the cost savings with leuprorelin acetate Atrigel against leuprolide acetate microsphere, goserelin, and triptorelin were 8243.54 TL, 4861.84 TL, and 9098.58 TL, respectively, for patients with a testosterone suppression target of <20 ng/dL and 5840.38 TL, 913.63 TL and 5056.03 TL, respectively, for patients with a testosterone suppression target of <50 ng/dL. For all study patients, leuprorelin acetate Atrigel provided cost savings of 8386.04 TL, 3710.79 TL, and 8446.64 TL against leuprolide acetate microsphere, goserelin, and triptorelin, respectively, in patients with a testosterone suppression target of <20 ng/dL and 479.41 TL, 1142.13 TL, and 5490.79 TL, respectively, in patients with a testosterone suppression target of <50 ng/dL.

A deterministic sensitivity analysis was performed using 75% and 125% as low and high values, respectively, of all relevant input parameters. If the parameter uncertainty was unknown, a standard 25% variation was used. Sensitivity analyses also showed that leuprorelin acetate Atrigel was superior to its comparators by means of ICER values at low- and high-sensitivity margins.

## Discussion

Prostate cancer is second-leading cancer among males in Turkey, which has a significant economic burden on the healthcare systems. The Republic of Turkey Ministry of Health reported that the incidence rate of prostate cancer in males was 32.9 per 100.000 popu-

lation in 2014.2 which means that more than 26.000 individuals are diagnosed with prostate cancer each year. When the excellent survival rate in this disease is considered, together with the high incidence rate, there is a growing share of costs related to the treatment of prostate cancer among all healthcare expenditures. From this point of view, determining the cost-effectiveness of currently available therapeutic methods is crucial for guiding both regulatory authorities and physicians. Based on this necessity, we conducted a comprehensive cost-effectiveness analysis to evaluate the leuprorelin acetate Atrigel, in comparison with other available LHRH agonists in the market. Overall, we found that leuprorelin acetate Atrigel was both clinically and economically superior to other comparators, such as leuprolide acetate microsphere, goserelin, and triptorelin, which yielded the conclusion that leuprorelin acetate Atrigel was the most cost-effective LHRH agonist in the market.

The analyses of our study were conducted for patients with intermediate and high risk, as well as for target testosterone levels of <20 ng/dL and <50 ng/dL. The risk stratification directly affects duration, and target testosterone levels are directly associated with the achievement of pharmacological castration and patient outcomes, which all eventually affect the cost of treatment. Target testosterone levels that should be achieved for castration is reported to be <20 ng/dL11; however, regulatory authorities and clinical trials still use a testosterone target of <50 ng/dL for castration. Overall, we found that leuprorelin acetate Atrigel provided significantly greater clinical effectiveness in terms of LYGs and superior economic efficiency concerning ICER values compared to other LHRH analogues.

When all patients with prostate cancer were considered without risk stratification, in patients who achieved a target testosterone level of <20 ng/dL with leuprorelin acetate Atrigel compared with leuprolide acetate microsphere, goserelin, and triptorelin, LYGs were 0.46 years, 0.35 years, and 0.55 years, respectively, and cost savings were 8386.04 TL, 3710.79 TL, and 8446.64 TL, respectively. In patients who achieved a target testosterone level of <50 ng/dL, LYGs were 0.53 years, 0.36 years, and 0.70 years, respectively, and cost savings were 5479.41 TL, 1142.13 TL, and 5490.79 TL, respectively. Based on these calculations, leuprorelin acetate Atrigel can be accepted as the treatment of choice among currently available LHRH analogues.

Currently, ADT with LHRH agonists is the recommended first-line treatment for symptomatic and asymptomatic patients with advanced disease, as well as for symptomatic patients with locally advanced disease. Among LHRH agonists and leuprorelin or leuprolide acetate preparations, leuprorelin acetate Atrigel has a unique polymeric delivery system that provides a continuous administration of leuprolide acetate during biodegradation of the leuprorelin depot. In Europe, there are three commercially available forms of leuprorelin acetate Atrigel, which contain 7.5 mg, 22.5 mg, and 45 mg doses for 1-, 3- and 6-months of administration interval, respectively. A previous study that evaluated the economic impact of different preparations of leuprolide acetate in the management of advanced prostate cancer reported that the 6-month depot formulation of leuprorelin acetate Atrigel was found to be the most cost-effective treatment option, despite its higher unit price.[17] Another study that evaluated the efficacy, safety, and costs of treatment with 1-, 3- and 6-monthly depot formulations of leuprolide acetate in ADT for prostate cancer in nine European countries (Austria, Belgium, Czech Republic, Hungary, Italy, Latvia, Netherlands, Poland, and Portugal) reported that these leuprorelin acetate Atrigel formulations provided similar efficacy and safety; however, the 6-month formulation offered the greatest cost savings and could be considered the treatment of choice in eligible patients. [18] In the present study, different formulations of leuprorelin acetate Atrigel were not evaluated. However, considering our findings in conjunction with the currently available literature, long-depot formulation of leuprorelin acetate Atrigel can be suggested as the treatment of choice in prostate cancer compared with other leuprolide acetate preparations in the market.

The present study has some limitations. First, the number of patients using leuprorelin acetate Atrigel is relatively low in comparison with other LHRH analogues. This may be considered as a lack of power of the study. However, individual, patient-based cost calculations and standardization of the initial assumptions for treatment, like a biopsy, or duration of treatment in separate risk groups and target testosterone levels, can waive the concerns about the study power. Second, only direct medical costs were estimated in our cost-effectiveness model. Nevertheless, the cost of cancer treatment includes direct costs and nonmedical costs like out-of-pocket expenditures, indirect costs (such as productivity loss), and psychosocial costs (such as quality-of-life loss).[19] However, as literature data support that leuprorelin acetate Atrigel is associated with patient satisfaction in the treatment of locally advanced and metastatic prostate cancer,[20] we prioritized the estimations and cost-effectiveness of direct medical costs

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related with leuprorelin acetate Atrigel and other LHRH analogues from the perspective of buyers in Turkey. The literature also supports this assumption, as the 6-month depot formulation of leuprorelin acetate Atrigel has been reported to be associated with reduced anxiety, decreased emotional burden, improved flexibility with scheduling, less frequent injections, improved comfort, fewer doctor visits, decreased site reactions, decreased cost, fewer missed visits, and in theory, decreased risk of a breakthrough.[21] Moreover, as the indirect costs may vary from country to country, the direct costs may provide more robust figures for further comparisons among various healthcare systems. Another limitation of this study is the standardization of treatment-associated factors for each patient. However, as mentioned previously, this standardization provides more robust estimations of direct costs of each treatment option, as well as more robust comparisons of both clinical and economical effectiveness measures.

## Conclusion

According to the results of this cost-effectiveness analysis, leuprorelin acetate Atrigel was clinically more effective compared with other LHRH analogues in intermediate- and high-risk patients, as well as in all patients in any risk group, when the testosterone suppression target was <20 ng/dL or <50 ng/dL. For intermediate-risk patients, high-risk patient, and all patients in any risk group, leuprorelin acetate Atrigel was cost-saving compared with other LHRH analogues, whether the testosterone suppression target was <20 ng/dL or <50 ng/dL. These clinical and economic findings show that leuprorelin acetate Atrigel can be considered the treatment of choice in prostate cancer.

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**Authorship contributions:** Concept – G.O; Design – G.O.; Supervision – F.A.; Funding – Astellas Pharma Turkey; Materials – G.O.; Data collection and/or processing – G.O; Data analysis and/or interpretation – G.O., F.A.; Literature search – G.O.; Writing – G.O., Ş.D.; Critical review – G.O.

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