Switching from an LHRH Antagonist to an LHRH Agonist: A Case Report of 10 Finnish Patients with Advanced Prostate Cancer

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ABSTRACT

Introduction: Luteinizing hormone-releasing hormone (LHRH) analogues are widely used for the treatment of advanced hormone-dependent prostate cancer. However, there are currently no clinical guidelines for switching between LHRH analogues. It has been reported that there may be clinical benefits for patients switching between different formulations of LHRH agonists, as well as from an LHRH agonist to LHRH antagonist, but there are no published data on switching from an LHRH antagonist to an LHRH agonist. In this paper, we summarize the clinical notes of 10 patients with hormone-sensitive advanced prostate cancer who switched from an LHRH antagonist to an LHRH agonist.

Methods: Patients with T3N0M0–T4N1M1 prostate cancer experiencing injection site reactions, such as pain and swelling, with monthly degarelix (Firmagon®) subcutaneous injections were switched to the 3-monthly leuprorelin acetate implant (Leuprorelin Sandoz®) subcutaneous injections.

Results: Mean patient age was 75 years (SD 8.3; range 59–85) and Gleason scores ranged from 7 to 9. The mean [± standard deviation (SD)] duration of degarelix treatment was 5 ± 3.7 months (range 2–13). After switching, prostate serum antigen levels were comparable or reduced from those measured prior to switching, showing that efficacy was not compromised. Throughout the course of treatment, no patients reported injection site reactions. Patients reported increased satisfaction with the leuprorelin acetate implant versus degarelix, mainly because of a lack of injection site reactions and reduced frequency of injection.

Conclusion: This is the first report of the clinical experience and potential cost implications of switching from an LHRH antagonist to an LHRH agonist. These data are consistent with other experiences of switching between LHRH analogues in terms of efficacy, safety, and potential cost savings, and provide preliminary evidence that the switch from an LHRH antagonist to an agonist is safe and equally efficacious.

Keywords: Case report summary; Degarelix; Leuprorelin acetate; LHRH analogues; Prostate cancer; Switching
INTRODUCTION

Androgen deprivation therapy (ADT) is still the mainstay of treatment for advanced hormone-dependent prostate cancer, with the main form being luteinizing hormone-releasing hormone (LHRH) agonists, such as goserelin acetate and leuprorelin acetate [1]. If permanent castration is required, orchiectomy is the most cost-effective and effective treatment option, but is very seldom used in clinical practice in Western countries.

Luteinizing hormone-releasing hormone (LHRH) agonists bind to the LHRH receptor and stimulate luteinizing hormone (LH) and follicle-stimulating hormone (FSH) secretion. Chronic exposure leads to downregulation of LHRH receptors, thereby suppressing LH and FSH secretion, and ultimately inhibiting testosterone production. Castration levels of testosterone with LHRH agonists are typically achieved within 2–4 weeks [2]. LHRH antagonists, such as degarelix, are an alternative form of ADT. They inhibit LHRH receptors, leading to a rapid decrease in LH, FSH, and testosterone levels, without the testosterone flare associated with LHRH agonists [2].

Clinical trials have compared the effects of LHRH agonists and LHRH antagonists on prostate-specific antigen (PSA) and testosterone levels, but large comparative trials are needed to provide overall survival and/or progression-free survival data [3]. Previous studies have also reported LHRH agonists and LHRH antagonists to be generally well tolerated (with most adverse events being consistent with androgen suppression or the underlying condition), with the exception of reactions at the injection site with LHRH agonists [4–8].

Switching between hormonal therapies has been reported to have clinical benefits [6, 8–10]. There are currently no clinical guidelines for switching between LHRH analogues [2, 11, 12], but it has been reported that there could potentially be clinical benefits for patients if they switch between the different formulations of LHRH agonists [8] as well as from an LHRH agonist to LHRH antagonist [6, 10]. There have, however, been no published data reported for switching from an LHRH antagonist to an LHRH agonist. Here we summarize the clinical notes of 10 patients with hormone-sensitive advanced prostate cancer who switched from an LHRH antagonist to an LHRH agonist.

CASE PRESENTATION

Ten patients with T3N0M0–T4N1M1 prostate cancer experiencing injection site reactions, such as pain and swelling, with monthly degarelix (Firmagon®) subcutaneous injections were included within this collection of 10 case studies (Fig. 1). Mean patient age was 75 years [standard deviation (SD) 8.3; range 59–85] and Gleason scores ranged from 7 to 9 (Table 1). All patients provided informed consent and the study was carried out in accordance with ethical standards and Good Clinical Practice.

Primary treatment for prostate cancer was external beam radiation therapy \( (n = 9) \) or chemical castration \( (n = 1) \). The mean (± SD) duration of degarelix treatment was 5 ± 3.7 months (range 2–13). The first patient was switched to the leuprorelin acetate implant \( (\text{Leuprorelin Sandoz}^\text{®}) \), with no antiandrogen therapy, in December 2015 and the mean duration of treatment is currently 7 months (range 4–10). Of the 10 patients who switched from degarelix, three received the leuprorelin acetate implant before radiotherapy as neoadjuvant therapy and the seven men who received it as adjuvant therapy are still receiving the implant (Fig. 1). PSA levels were measured before and after switching treatments [time to post-switch PSA measurement, 1–6 months, mean 2.2 ± 1.6 (SD)]. PSA levels were comparable or reduced from those measured prior to switching, showing that efficacy was not compromised (Fig. 2). Mean PSA level before switching was 6.1 ± 9.1 versus 4.4 ± 6.7 ng/mL after switching.

Throughout the course of treatment, no patients reported injection site reactions, such as pain or swelling, with the leuprorelin acetate implant. Patients reported increased satisfaction with the leuprorelin acetate implant than with
degarelix, mainly because of a lack of injection site reactions and reduced frequency of injection. Moreover, the 3-month injection interval with the leuprorelin acetate implant was reported by the patients to be preferable to the monthly interval of degarelix. Following the switch to the leuprorelin acetate implant in the adjuvant setting, all seven patients stated that they preferred to continue with this therapy.

In Finland, continuous treatment with the leuprorelin acetate implant also appeared to be more cost-effective due to reduced costs (decreased from €517 for 3 months treatment with degarelix to €316 for the leuprorelin acetate implant). In addition, costs associated with nurse involvement were reduced to one-third of the original cost due to less frequent administration of injections.
SUMMARY AND CONCLUSIONS

This is the first report of the clinical experience and the potential for associated cost savings when switching men with advanced prostate cancer from an LHRH antagonist to an LHRH agonist. The recurrent injection site reactions experienced by all 10 Finnish patients who initially received degarelix could be attributed to the associated histamine release from mast cells, which has been associated with all LHRH antagonists [13]. The data reported here for men switching from degarelix to the leuprorelin acetate implant are consistent with other switching experiences between LHRH analogues in terms of efficacy and safety [6, 8, 10] as well as the potential for associated cost savings [1]. The case report presented here, therefore, provides preliminary evidence that the switch from an LHRH antagonist to an agonist is safe and equally efficacious. However, a prospective patient preference study reporting local adverse effects would be useful to support these findings, as well as a large comparative trial to compare overall survival and/or progression-free survival of LHRH agonists and LHRH antagonists [3].

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Compliance with Ethics Guidelines. All patients provided informed consent and the study was carried out in accordance with ethical standards and Good Clinical Practice.

Data Availability. The datasets during and/or analyzed during the current study are available from the author on reasonable request.

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