Rev Mex Urol. 2016;**76(6)**:346–351

Revista Mexicana de
UROLOGIA
ÓRGANO OFICIAL DE DIFUSIÓN DE LA SOCIEDAD MEXICANA DE UROLOGÍA
www.elsevier.es/uromx

ORIGINAL ARTICLE

Evaluation of efficacy of buserelin plus nilutamide in Mexican Male patients with advanced prostate cancer

R.F. Velázquez-Macías[a,*], S. Aguilar-Patiño[b], R. Cortez-Betancourt[c], I. Rojas-Esquivel[d], G. Fonseca-Reyes[e], N. Contreras-González[f]

[a] *Servicio de Urología, Hospital Regional Lic, Adolfo López Mateos, Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado, Distrito Federal, Mexico*
[b] *Servicio de Urología, Hospital General Vasco de de Quiroga, Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado, Morelia, Michoacán, Mexico*
[c] *Servicio de Urología, Centro Médico Nacional 20 de Noviembre, Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado, Distrito Federal, Mexico*
[d] *Servicio de Urología, Hospital Regional 1 de Octubre, Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado, Distrito Federal, Mexico*
[e] *Servicio de Urología, Hospital Regional General Ignacio Zaragoza, Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado, Distrito Federal, Mexico*
[f] *Servicio de Urología, Hospital General Tacuba, Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado, Distrito Federal, Mexico*

Received 6 July 2016; accepted 7 October 2016
Available online 18 November 2016

KEYWORDS
Buserelin;
Nilutamide;
Advanced prostate cancer;
Androgen-deprivation therapy

Abstract
Introduction: In recent years, total androgen blockade therapy for advanced prostate cancer has been a reasonable option to castration due to the discovery and development of new pharmacologic agents. In this study, our aim was to evaluate the efficacy of the combined treatment of nilutamide plus buserelin and to describe the occurrence of adverse events associated with this treatment.
Material and methods: A descriptive, prospective study was conducted. Patients with advanced prostate cancer receiving nilutamide plus buserelin were evaluated at 3, 6, and 9 months. The primary endpoint was the reduction of serum levels of prostate-specific antigen (PSA).
Results: One hundred and four patients were included in the study, but only 67 patients had complete information and thus were evaluated in the efficacy analysis: 65 (97.0%) achieved a 50% reduction in PSA level, compared with the baseline value, and 2 patients achieved a

* Corresponding author at: San Faustino M842, L12, Pedregal Santa Úrsula, CP 04600 Ciudad de México, Mexico. Tel.: +52 5585810069.
E-mail address: ravelma@urocirugia.com (R.F. Velázquez-Macías).

http://dx.doi.org/10.1016/j.uromx.2016.10.001

decrease <10 ng/ml. The combination therapy was well tolerated, given that only 7 patients (6.7%) presented with mild adverse events that did not require treatment suspension or other specific maneuvers.
Conclusions: Treatment with nilutamide plus buserelin appears to be safe and effective in controlling tumor activity in advanced prostate cancer patients.

PALABRAS CLAVE
Buserelina;
Nilutamida;
Cáncer prostático avanzado;
Terapia de privación androgénica

Evaluación de la eficacia de buserelina más nilutamida en pacientes mexicanos con cáncer prostático avanzado

Resumen
Introducción: En años recientes la terapia de privación máxima de andrógenos para el cáncer avanzado de próstata constituye una opción razonable a la castración debido al descubrimiento y desarrollo de nuevos agentes farmacológicos. En este estudio nuestro objetivo fue describir la eficacia del tratamiento combinado de nilutamida más buserelina y la ocurrencia de efectos adversos asociados con este tratamiento.
Material y métodos: Se realizó un estudio descriptivo, prospectivo, en pacientes con cáncer de próstata avanzado, los cuales recibieron nilutamida más buserelina y fueron evaluados a los 3, 6 y 9 meses. El desenlace primario fue el descenso del nivel sérico de antígeno prostático específico.
Resultados: Se incluyeron 104 pacientes, pero solo 67 fueron considerados porque tuvieron información completa: 65 (97%) lograron un descenso del 50% del antígeno prostático específico en comparación con el inicial; 2 pacientes lograron un descenso < 10 ng/mL. El tratamiento fue bien tolerado ya que solo 7 reportaron efectos adversos (n = 104); estos fueron leves y no requirieron suspender el tratamiento u otras maniobras específicas.
Conclusiones: El tratamiento con nilutamida más buserelina fue seguro y efectivo para controlar la actividad tumoral en pacientes con cáncer de próstata avanzado.

Introduction

Prostate cancer (CaP) is the most common cancer in men.[1] In Mexico, it is the second cause of cancer-related mortality.[2] Even though prostate-specific antigen (PSA) screening has led to some over-diagnosis and over-treatment of CaP in younger men, older men tend to have more aggressive tumors and few receive curative therapy, thus explaining the high mortality rate.[3] Furthermore, 26–34% of patients will be diagnosed at an advanced stage of the disease.[4]

Androgen-deprivation therapy (ADT) is the standard approach for the first-line treatment of advanced CaP.[5] ADT can be achieved with the use of hormonal therapy or through surgical castration.

Androgens have a stimulating effect on the androgen receptors within the epithelial cells of the prostate. Once the hormones are located intracellularly, they are converted into dihydrotestosterone (DHT) by 5-alpha reductase. DHT is the most active form of testosterone and carries most of the hormonal functions, including cell replication.[6] Thus, ADT induces apoptosis in susceptible CaP cells by reducing the synthesis of androgens and their interaction with the androgenic receptor.[7]

ADT is usually achieved through the use of luteinizing hormone-releasing hormone analog or a gonadotropin-releasing hormone agonist, such as buserelin.[8] These drugs must be combined with antiandrogens, such as bicalutamide or nilutamide (which block the binding of DHT to the androgen receptor in the nucleus of CaP cells), to completely block the effect of testosterone.[9]

Whenever these drugs are used in combination, the resulting therapy is called maximum androgen blockade (MAB).[10]

Nilutamide is a nonsteroidal androgen receptor antagonist that shows affinity for androgen receptors, but not for other steroid receptors. It has a low adverse event profile consistent with androgen depletion (hot flushes, gynecomastia, impotence, and gastrointestinal disturbances), and has been shown to exert a significant PSA response in advanced CaP patients.[11]

Buserelin is a synthetic luteinizing hormone-releasing hormone analog. Its intermittent administration stimulates the release of luteinizing hormone and follicle-stimulating hormone, thus increasing testosterone concentrations in males, whereas its continuous administration suppresses secretion of both LH and FSH, resulting in a drop in testosterone concentrations. Its adverse event profile