



## ORIGINAL ARTICLE

# Cognitive function in patients on androgen suppression: A prospective, multicentric study<sup>☆</sup>



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### KEYWORDS

Luteinizing hormone-releasing hormone analogs;  
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### Abstract

**Objective:** To assess the effect of androgen deprivation therapy (ADT) on cognitive performance (CP) in patients with prostate cancer (PCa) after 6 months of treatment with luteinizing hormone-releasing hormone (LHRH) analogs.

**Material and methods:** Prospective, observational, multicentre, open-label study of patients diagnosed with nonmetastatic or asymptomatic metastatic PCa scheduled to receive LHRH analogs for  $\geq 6$  months. We assessed four CP domains at baseline and after 6 months of ADT: (1) Working memory: Wechsler Adult Intelligence Scale III (WAIS III) Digit Span Subtest (WAIS III-Digit); (2) Visual memory: ad hoc visual memory test; (3) Visuospatial ability: Judgment of Line Orientation (JLO) and Mental Rotation of Three-Dimensional Objects (3D-Rotation); and (4) Nonverbal analytical reasoning: WAIS III Matrix Reasoning Test (WAIS III-MRT). Changes outside the baseline 95% confidence intervals were considered significant.

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**PALABRAS CLAVE**

Análogos de la hormona liberadora de la hormona luteinizante;  
Cáncer de próstata;  
Supresión androgénica;  
Función cognitiva

**Results:** A total of 308 patients completed the study. Of these, 245 (79.6%) experienced no statistically significant changes on any test and 63 patients (20.4%) experienced significant changes in  $\geq 1$  test. Of these, most presented a change in only one test, distributed evenly between improvements (58 patients; 18.8%) and worsening (56 patients; 18.2%). For individual tests, most patients (87.8–91.8%) had no change from baseline; however, the significant changes (improvement vs. deterioration, respectively) were as follows: WAIS III-Digit (6.3% vs. 5.9%); visual memory (5.3% vs. 5.7%); JLO (5.3% vs. 4.5%); 3D-Rotation (4.1% vs. 4.1%); and WAIS III-MRT (4.8% vs. 5.8%).

**Conclusions:** CP in patients with PCa does not appear to be adversely affected by 6 months of LHRH analog administration.

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### Función cognitiva en pacientes tratados con supresión androgénica: estudio prospectivo y multicéntrico

#### Resumen

**Objetivo:** Evaluar el efecto de supresión androgénica sobre la función cognitiva de pacientes con cáncer de próstata (CP) tras 6 meses de tratamiento con análogos de la hormona liberadora de la hormona luteinizante.

**Material y métodos:** Estudio prospectivo, observacional, multicéntrico y abierto de pacientes con CP programados para recibir análogos de la hormona liberadora de la hormona luteinizante durante  $\geq 6$  meses. Evaluamos 4 dominios de la función cognitiva antes del tratamiento y tras 6 meses: 1) memoria de trabajo: Escala Wechsler de inteligencia para adultos (WAIS III-dígito); 2) memoria visual: prueba de memoria visual; 3) capacidad vídeo-espacial: juicio de orientación de línea y rotación mental de objetos tridimensionales (rotación-3D); y 4) razonamiento analítico no verbal: WAIS III-MRT. Se consideraron mejorías o empeoramientos significativos cuando existió un cambio fuera del valor definido por el intervalo de confianza del 95% de la valoración basal de cada prueba.

**Resultados:** De los 308 pacientes que completaron el estudio, en 245 (79,6%) no se observaron cambios significativos en ninguna prueba y en 63 pacientes (20,4%) se observaron cambios significativos en una prueba o más. De estos últimos la mayoría presentó un cambio en una sola prueba, distribuida uniformemente entre mejorías (58 pacientes; 18,8%) y empeoramientos (56; 18,2%). En la mayoría de pacientes (87,8-91,8%) no se observaron cambios significativos en las pruebas individuales respecto a sus niveles basales. El porcentaje de pacientes con cambios significativos (mejoría vs. deterioro, respectivamente) fue: WAIS III-dígito (6,3% vs. 5,9%); memoria visual (5,3% vs. 5,7%); juicio de orientación de línea (5,3% vs. 4,5%); rotación 3D (4,1% vs. 4,1%); WAIS III-MRT (4,8% vs. 5,8%).

**Conclusiones:** El estado cognitivo de los pacientes con CP no parece verse afectado por 6 meses de tratamiento con análogos de la LH.

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## Introduction

More than one third of all men diagnosed with prostate cancer (PCa) receive androgen deprivation therapy (ADT), typically luteinizing hormone-releasing hormone (LHRH) analogs.<sup>1</sup> ADT is indicated as primary systemic therapy in advanced disease and as neoadjuvant, adjuvant, or concomitant therapy in conjunction with radiation therapy in localized or locally-advanced PCa.<sup>2</sup> The benefits of ADT are well-established, including a reduction in prostate-specific antigen (PSA) levels and, most importantly, an increase in overall survival.<sup>2</sup>

Despite the clear benefits of LHRH analogs, these drugs are not without adverse effects, most of which are well understood.<sup>3</sup> By contrast, the effect of castration on

cognitive function in PCa patients has received relatively little attention. Consequently, the impact of ADT on cognitive performance (CP) remains unclear due to the inconclusive and often contradictory findings reported to date.<sup>4</sup> Nevertheless, interest in this topic has been increasing in recent years, as evidenced by the growing, but still limited, number of published studies. Unfortunately, all the studies published to date have consisted of small sample sizes (18–77 patients).<sup>5–13</sup> The largest prospective study conducted to date<sup>10</sup> found that ADT had no significant impact on cognitive function, although other studies have reported ambiguous findings, with deterioration in some cognitive functions but improvement in others.<sup>11,14</sup> These highly heterogeneous and inconsistent results are attributable, at least partially, to the lack of large prospective studies.

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